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CENTRAL OFFICE OF INFORMATION. Reference Pamphlet No. 20. **Health Services in Britain.** 2nd Edition. 56 pp. 1959. London: H.M. Stationery Office. [3s. 6d.]

As expected when the first edition appeared in 1957 [for a summary, see this *Bulletin*, 1957, v. 32, 633] a new one has been quickly needed. It is well written, comprehensive and short; it includes this time a little comment on why certain things have been done or not done.

Though in the main it is an account of the National Health Service there are also chapters on Public Health (environmental services), the School Health Service, Industrial Health, Medical Research and Professional Training.

The differences, mostly in the administrative structure of the National Health Service in England and Wales, in Scotland and in Northern Ireland are described.

There is a good account of the basic principles which govern the payments made to general practitioners for their services but, probably wisely, no attempt is made to explain the complex working of the "Central Pool" from which doctors are paid.

As a general description of the Health Services of Britain it is excellent and is highly recommended as a gift for visiting foreigners.

Only two errors were discovered: on page 18 "surgical medicine" appears presumably for "physical medicine" and in the list on page 48 of research units the Jessop Hospital for Women is stated to be in Leeds instead of Sheffield. *Allen Daley*

BACH, H. E., ROSS, O., LAING, B. S., HARRIS, D., STOCKER, A. H., STEWART, G. G., BROWN, F. G., GRAHAM, J. & TAYLOR, S. **The Health Centres of Harlow. The Second Phase.** *Lancet.* 1958, Nov. 15, 1055–60, 4 figs.

The authors are 3 general practitioners and 2 dental surgeons who work at the Harlow Health Centres, 3 administrative medical officers from the Essex County Council and the regional hospital board together with Lord Taylor (until recently Dr. Stephen Taylor) who is a member of the Development Corporation who are building the New Town of Harlow.

For a summary of the first phase see this *Bulletin*, 1956, v. 31, 97.

There are now 9 buildings from which the health services of the town are provided: 5 function as health centres though not built under the provisions of the National Health Services Act 1946; an industrial health centre; a building for specialist children's services; a child guidance centre and a temporary out-patient department containing provision for general practitioner pathology and radiology. The buildings will be completed by the provision of a new hospital, another local health centre making 6 in all, and another industrial health centre making 2. Apart from the new hospital, the buildings erected or to be erected will cost just over £250,000 provided by the Nuffield Provincial Hospitals Trust. A rent of 6% of the capital cost, based on floor space occupied, is charged to the users.

A map shows the lay-out of the town and the location of the various buildings.

An important lesson learnt is that efficiency and economy result when the sponsoring body fixes the global sum available for a building and leaves the details to the local people. Another is that fixing the rent on the basis of floor space occupied leads to a readiness to share the space with others who will contribute to the rent. Planning, particularly with multiple use in mind, must be a joint exercise of architect, users and administrator. Lord Taylor has acted as co-ordinator and a Building Committee, which would have had to be large and delay-producing, has not been needed.

The population of Harlow is now over 42,000 which is about one-half the projected total. There are 69 factories and 20 schools.

The article contains clear plans of the various clinic buildings. A group of buildings near the site of the proposed hospital provides not only a local health centre for general medical and dental practice and local authority services, but also a child guidance centre and a temporary out-patient department with 11 consulting sessions a week which will be transferred to the new hospital when it is ready in about 3 years. One of the new local health centres to house 6 doctors, 4 dentists, local authority maternity and child welfare clinics and a caretaker cost only £32,000.

There are 7 "immediate conclusions". The main ones are that "good general practice in a town is essentially group practice"; general practitioners and dentists in the National Health Service should work together in the same building but retain their own autonomy; the centres must be built and ready by the time the new residents move into the new town or estate; the doctors must have no other place of practice in the town and should be protected against "extra-health centre" competition.

[This is a most promising experiment which should be studied by all interested in the future of public health or general practice.] *Allen Daley*

CANADIAN J. PUB. HEALTH. 1959, Feb., v. 50, No. 2, 45–59. **The Public Health Significance of Recent Legislation in the Fields of Hospital Insurance and Home Care. A Symposium.**

The recent "Hospital Insurance and Diagnostic Services Programme" of Canada is leading to an examination of its effects on home care and on the work of provincial and local public health departments.

The symposium was held during the annual meeting of the Ontario Public Health Association in October, 1958.

Dr. K. C. CHARRON (pp. 45–47), the Federal Director of Health Services, expressed the belief that enrolment for the insurance plan would start with 85% of the total population and rapidly increase. The plan covers both in-patient and out-patient hospital services. The ownership and management of the hospitals will remain in local hands. Coordination of hospital and home care is essential and several pilot projects in home care now in operation are being studied.

Dr. R. W. I. URQUHART (pp. 47–49), the chairman of the Ontario Hospital Services Commission, pointed out that the commission was an independent administrative authority which reported to the Parliament of the Province through the Minister of Health. The Commission has not taken over the hospitals but it encourages, counsels and guides local hospital boards and is anxious to develop integration between the hospitals and the public health and welfare agencies.

Miss D. G. GARDNER (pp. 50–51), the Chief Supervisor of the Homemakers and Nurses Services of the Ontario Department of the Public Welfare said development of domestic help and home nursing programmes by the municipalities was needed and to start with they would have to use existing voluntary organizations now active in these fields.

Dr. Robert J. GALLOWAY (pp. 51–53), gave the point of view of a practising doctor, a surgeon. "Health, though a social problem, is an individual's problem" and the doctor-patient relationship must stand firm. Practising doctors must work under a free enterprise system. There was misconception and some danger in the use of the word "free" treatment for an insurance system which, in fact, did not mean that it cost nothing but only that the cost was charged in advance by the premium.

Miss Louise MINER (pp. 53–57), Public Health Nursing Supervisor, Saskatchewan Department of Public Health, described the nursing service which started in 1946. There was a growing demand for more hospital beds, more doctors, more nurses and more public health services. In each the demand has overtaken the supply. Nurses should be relieved of work which could be done by those with lesser skills and should be provided with assistants and clerical help. Liaison between hospitals and public health departments had improved and frequently public health nursing offices were located in hospitals. There is a danger that a larger proportion of the money available for health purposes will be spent on treatment and not leave enough for effective preventive work. In her Province home care services are not being used to capacity because the people prefer "free" care in hospitals.

Dr. Charlotte M. HORNER (pp. 57–60) the MOH of a Health Unit covering 1,363 square miles, reported on a 3½-year project to study an integrated programme of combined home and public health nursing. In one rural area home nursing took about 44% of the time of the home-public health nurse and assistance had to be obtained for the home nursing to enable the public health nursing to be done properly.

The general impression given by the symposium is that extension of the hospital insurance scheme will lead to more hospitalization and, for financial and other reasons, home nursing and preventive measures will need to be expanded or the hospital load will prove to be too heavy. It is curious that no one mentioned the "hotel" charge for hospital accommodation included in the Beveridge report but never applied in Britain. *Allen Daley*

ROYAL SOC. PROMOTION HEALTH J. 1958, July–Aug. & Sept.–Oct., v. 78, Nos. 4 & 5. **Health Congress at Eastbourne, April 28–May 2, 1958.**

The Congress was held in Eastbourne from April 28 to May 2 1958, and the inaugural address was contributed by the Minister of Health, in which he touched on the problems of old age, mental illness and dental health.

The following sections were reported:—

Food and Nutrition. There was a symposium on food additives, and legal, technological and biological matters were discussed, by J. R. NICHOLLS, F. H. BANFIELD and J. M. BARNES respectively.

Public Health Inspectors, in which there was a paper on food hygiene regulations and their extension to crown property and the licensing of vehicles, by S. MILLWARD.

Architecture and town planning, with a paper by G. W. MULLETT on architectural problems relating to the use of ionizing radiations, and one on planning and good taste.

The World Health Section, with an appreciation of WHO by Sir John CHARLES, a paper on world sanitation by H. G. BAITY, and one on world problems of sanitation by P. C. G. ISAAC.

The Mental Health Section, with a paper on the Royal Commission on the Law relating to Mental Illness and Mental Deficiency by T. P. REES, and others by L. T. HILLIARD and K. A. SOUTAR.

The Housing and Estate Management Section with a

paper on the unsatisfactory tenant by A. W. DAVEY and one on rural housing by C. W. N. MILES.

The Health and Welfare of the Family Section, introduced by Sir Arthur MASSEY and containing a symposium on society and its older members, to which papers were contributed by J. H. SHELDON, D. NEWMAN, Mrs. N. H. STRICKLAND and G. WYNNE GRIFFITH.

The Hospitals Section with papers on the out-patient departments and the welfare of out-patients, by A. G. EMSLIE, J. FRY and E. H. HURST.

The Health Education Section, which is represented by the Presidential Address by A. A. MONCRIEFF, and by a symposium on dental disease, the last great epidemic.

The Engineers and Surveyors Conference, which discussed the safe disposal of waste from atomic energy establishments, and road safety.

The Occupational Health Section in which problems of fatigue were discussed by Sir Frederic BARTLETT, E. JAQUES and D. CURRAN.

The Preventive Medicine Section in which there was a symposium on influenza.

The Conference of Public Health Inspectors, with papers on air pollution and meat inspection, and on housing.

The Conference of Medical Officers of Health with a symposium on the epidemiology of non-infective diseases, including mental disorders.

The Veterinary Hygiene Section, with a symposium on lesser-known bacterial, virus and parasitic infections common to animals and man.

The Tropical Hygiene Section with a presidential address by Sir James KILPATRICK and a paper on amoebiasis, both of which are reviewed in full in the *Tropical Diseases Bulletin*, [1959, v. 56, 676].

It is not practicable to do more than indicate the scope of this Congress. The papers, and the discussions they provoked, should be read in full.

Charles Wilcocks

SHILOH, A. **Middle East Culture and Health.** *Health Education J.* 1958, Nov., v. 16, No. 4, 232–43.

This is a very perspicacious and informative essay in which the concepts and beliefs which exercise an overwhelming influence on behaviour with relation to disease are shown to be "logical expressions of a patterned system". The essential basis is that all illnesses or injuries are subjective affairs arising out of personal actions or caused by someone or something possessed with a power. There are two fundamental concepts pertaining to preventive and curative medicine, namely animism which is a belief in evil spirits, and animatism which is a belief in an impersonal power "which may exist latent in an individual or object and be utilized only by those aware of the correct method of tapping it".

Injuries affecting the "external body", though caused by an evil spirit or the evil eye, are treated on objective principles and the primary emphasis is on treatment; but for illnesses of the "inner body", which are concealed, the subjective beliefs in evil spirits and evil powers are paramount, and the primary emphasis is on prevention.

The author gives many illustrations of the ubiquity of evil spirits in the environment, and of the means used to ward them off. The whole of life is bounded and constricted by these beliefs, which are so strong that there can be no question of trifling with them. But like other authoritarian systems this set of rules satisfies the mind. There are practitioners who hear the details of illness, define it, name it (and thereby weaken it), and pronounce a positive prognosis to neutralize the evil forces. The patient then receives a rich fund of strength and is therefore emotionally able to endure the physical discomforts during the "official" course of curative treatment.

[This is a paper of the greatest importance; it adds point to the writings of those who have in Africa and elsewhere attempted to induce these traditional practitioners to accept and use at least some western methods and ideas without as yet discarding their own. It seems unlikely that an attitude of strong disapproval would do more than provoke hopeless resentment.]

Charles Wilcocks

Maternal and Child Health

LONDON SCHOOL OF HYG. & TROP. MED. **A Study Group of the Public Health Department. The Smoking Habits of School Children.** *Brit. J. Preventive & Social Med.* 1959, Jan., v. 13, No. 1, 1–4.

This report presents the results of the analysis of 3,479 simple questionnaires completed by 1,797 boys and 1,682 girls who were pupils at 2 grammar and 4 secondary modern schools in an industrial county borough near London. In all there were 3,853 pupils on the school's rolls of whom 313 were absent at the time of the survey. As 61 questionnaires were rejected because they were incomplete, the analysis is based on 90% of the population in the 6 schools. Questionnaires were completed in class by the pupils, the instructions and questions being read to them by their teachers; in 102 of the 127 classes involved the completed forms were collected by a member of the study group to preserve and emphasize that the answers were confidential. The following definitions were used: (1) as little as one puff of a cigarette was counted as "having smoked", (2) the smoking of 5 or more cigarettes a week was defined as "regular" smoking.

Smoking habits appeared to be related to age, sex and type of school; percentages of children who had smoked are shown for single years of age. In grammar schools these increased between ages 11 and 17 from 40·3 to 72·9% in boys and from 21·2 to 75·9% in girls. In secondary modern schools they increased between ages 11 and 16 from 71·1 to 89·5% in boys and from 38·0 at age 11 to 61·3% at age 15 in girls (the proportion at age 16, 36·4% is probably unreliable). In all, 8% of the children were classified as regular smokers as defined above, and similar age, sex and type of school variation was observed in the proportion of regular smokers as in the proportion having smoked. Thus of the grammar school children 1·9% of boys and 1·8% of girls aged 13 were classified as regular smokers compared with 21·3% of boys and 2·8% of girls of the same age in secondary modern schools. At age 17 in grammar schools this proportion was 27·1% for boys and 3·7% for girls and at age 15 in secondary modern schools it was 35·4% for boys and 5·0% for girls.

In all there were 260 boys aged 11–16 defined as regular smokers and if these are considered in 2 age-groups, 11–13 and 14–16, then as many as 7% of the younger sub-group and 12% of the older sub-group of regular smokers smoked 40 or more cigarettes per week. Of the 260 regular smokers, as many as 61% became regular smokers within one year of first having smoked and as many as 84% within 2 years.

The authors are of the opinion that the answers obtained were "relatively reliable" because they submitted 81 secondary modern school boys aged 11–15 to the questionnaire twice with an interval of 3 months and obtained roughly the same answers on each occasion. Thus on each occasion 68 said they had smoked and only one, who first said that he had not smoked, gave a different answer later. Moreover, 47% gave at each questioning the same age at which they first smoked, 39% gave a different answer by ± 1 year and 12·5% by ± 2 years. *E. A. Cheeseman*

NILSEN, E. **Smoking Habits among School Children in Norway.** *Brit. J. Preventive & Social Med.* 1959, Jan., v. 13, No. 1, 5–13, 2 figs. [13 refs.]

Pupils aged 13–20 years in various types of schools in Norway were questioned about their smoking habits. The sample consisted of 9,291 pupils from a total school population of some 140,000 and, although it does not represent the total population aged 13–20 years in Norway, efforts were made to make the sample representative of the school population of that age by sampling methods which are described in detail. Questionnaires were distributed to schools with instructions for teachers to read to their classes. Completed questionnaires were sealed in envelopes by the pupils before collection. No means of identifying replies and respondents existed so that in effect all information came to the research worker anonymously. Apart from questions about age, sex and school, the main question was framed to ask of the pupil "Do you smoke?"; he or she was required to answer "daily", "sometimes", "very seldom" or "never".

The proportion of boys who said they smoked daily increased from 3% at age 13 to 35% at age 19; for girls the corresponding increase was from 0% at age 13 (3% at 15) to 13% at age 19. Of the boys, 43% at age 13 and 37% at age 19 were non-smokers compared with 75% at age 13 and 47% at age 19 of the girls. It is believed that the age-groups 13–14 years are likely to give good estimates for the total, as distinct from the school population of that age. In that age-group occasional smokers (*i.e.* those who said they smoked "sometimes" or "very seldom") were more common in rural than urban schools. Thus 57% of boys and 36% of girls from rural schools at about this age, were classified as occasional smokers compared with about 46% of boys and 17·5% of girls in urban areas. There was little or no difference in the proportion of daily smokers of this age between urban and rural areas (about 5% of boys and 1% of girls). About 70% of the rural children said that one or both of their parents smoked compared with 81–85% of the urban children.

Among the children who said they were daily smokers the average number of cigarettes smoked per day was 4·2 for boys and 4·5 for girls aged 13 years and 12·0 for boys and 8·0 for girls aged 19 years.

Comparison of the results obtained by questionnaire, by interview of 261 children in the sample and from a Gallup poll undertaken by the Norwegian Cancer Society among adults, convinces the author that his results from the questionnaires are reliable, subject to the following reservations: (1) The analysis of questionnaires shows only the smoking habits at a given point in time so that some children may have previously tried smoking but had not continued. (2) The results are limited to children at school and there is some evidence that this underestimates the prevalence of the habit in all Norwegians aged 13–20 years. (3) There is some evidence that smoking is started at a younger age as time goes by and the present data show the situation only for 1957.

It is suggested that educational work to prevent smoking should be aimed at children aged 13 and continue until they are 18 because these are the ages during which smoking becomes habitual.

E. A. Cheeseman

POHOWALLA, J. N. & GHAI, O. P. **Common Accidental Poisonings in Children in Indore.** *Indian J. Child Health.* 1959, Apr., v. 8, No. 4, 205–12. [15 refs.]

This is a paper read at the annual conference of the Association of Pediatricians of India at Jaipur in January, 1959. There are very few publications on accidental poisonings of children in India and the study reported here was based on data obtained from the records of 2 hospitals in Indore. Out of approximately 10,500 children admitted to these hospitals in the 8-year period 1951–8, 136 were cases of accidental poisoning. A table sets out a classification of the nature of the poisoning and the chief signs and symptoms. Kerosene poisoning was the most frequent—41 cases with 2 deaths. Plants and seeds caused 37 poisonings and the chief ones in this group were *ratanjot* seeds (20 cases), castor seeds (7) and *Datura* seeds (8). Medicaments

of various kinds were responsible for 32 poisonings with opium coming first on the list with 20 cases and 1 death. Household substances including disinfectants caused 11 cases 5 of which were due to caustic soda; there were 9 cases of food poisoning and 6 cases in a miscellaneous group. The problem of accidental poisoning in children at different ages is discussed from the clinical aspect, from the point of view of causation of these accidents and also in comparison with the recorded experience of other countries [this *Bulletin*, 1958, v. 33, 924]. *M. E. Delafield*

BYERS, R. K. **Lead Poisoning. Review of the Literature and Report on 45 Cases.** *Pediatrics.* Springfield, Ill. 1959, Mar., v. 23, No. 3, 585–603, 8 figs. [50 refs.]

This is a useful review of the recent literature on lead poisoning which is followed by a report on 45 cases in the author's experience. In recent years *reported* cases of lead poisoning in children have increased considerably in number particularly in the United States because medical and public interest in the problem has come to be aroused by better diagnosis and other causes [this *Bulletin*, 1955, v. 30, 734; 1957, v. 32, 302].

The main source of lead poisoning in children is lead-containing paint ingested by those who have the pica habit which some authors state may be caused by a "disturbed mother-child relationship". Sections of the review cover recent papers on the absorption, distribution and storage of lead; abnormalities of porphyrin metabolism in lead poisoning and the pharmacology of edathamil disodium calcium. In a section on diagnosis there is a good discussion of the clinical aspects with emphasis on the importance of laboratory evidences which are: (1) microcytic anaemia with stippling, (2) X-ray abnormalities in the long bones and radio-opaque material in the gut, (3) coproporphyrin in the urine and increased free protoporphyrin in erythrocytes, (4) glycosuria with a normal blood sugar and (5) elevation of the total protein in the cerebrospinal fluid. Chemical proof of the intoxication may also be needful. The treatment of lead poisoning by edathamil is described. There is emphasis on the neurological sequelae in lead poisoning and also a long description of papers from Australia of "the possibility of late nephrosclerotic damage, years after lead poisoning" [this *Bulletin*, 1958, v. 33, 719].

The 45 cases of lead poisoning from the author's experience are fully described with a number of figures and tables. All the patients were treated with intravenous or intramuscular administration of edathamil during the acute stages. There is a warning that "Edathamil given orally in the presence of lead in the intestinal tract is a very dangerous drug." "With adequate treatment, half or more of the victims of lead poisoning should be returned to competitive life."

M. E. Delafield

Care of Old Persons and the Chronically Ill

MOSKOWITZ, E., FUHN, Edith R., PETERS, Margaret E. & KEARLEY, A. S. **Aged Infirm Residents in a Custodial Institution. Two-Year Medical and Social Study.** *J. Amer. Med. Ass.* 1959, Apr. 25, v. 169, No. 17, 2009–12, 1 fig.

In the medical and social study which is here described, a selected group of 115 aged, infirm individuals who were residents at a county home were observed over a period of 2 years. At the "custodial institution" these residents "received comprehensive medical care, including physical rehabilitation services provided by the county hospital" and social service was provided by the staff of the home. The individuals had been screened by a method of disability evaluation called "Physical Profile (PULSES)" which has previously been described (MOSKOWITZ and MCCANN, *J. Chron. Dis.*, 1957, v. 5, 342). Over the two-year period re-examinations were carried out at intervals of about 3 months and "a new physical profile was assigned [to] each patient to indicate his functional capabilities". During the period of study 36 individuals of the group died from causes which are stated. At the end of the 2 years "71·4% of the residents were at a level of complete independence, either in a wheel chair or on an ambulatory basis." In addition 7 were discharged to the community. There were no requests for readmission to the county home.

The age distribution of the individuals ranged from the groups 45 to 49 up to 95–99 years and of the total about 51% were over 75 years old. There is a description of the observed changes in the "Physical Profile." This system of disability classification "served as an effective index for recording the physical and mental status of the patients". *M. E. Delafield*

Social Medicine

DONGRAY, Madge. **Social Work in General Practice.** *Brit. Med. J.* 1958, Nov. 15, 1220–23.

This is a thoughtful and valuable account of an experiment started in the Darbishire House Health Centre in Manchester in June 1955. The author is a trained social worker with previous experience as a hospital almoner and in work in a child guidance clinic. She was attached whole-time to the Health Centre. 4 family doctors work at the Health Centre and between them they have 12,000 patients.

It is pointed out that, although social and family problems are often the real reason why a patient consults a doctor, the range and complexity of the present social services are such that few practising doctors can master the details as well as keep up with advances in clinical medicine. Some forms of illness produce family disharmonies of which the doctor has only a vague knowledge. The busy doctor seldom has the time to listen at length to the patient's story, particularly if it is long and involved, though often he can sense that there is deep-seated social trouble and refer its investigation to the social worker.

Examples are given of specific cases where the social worker was able to help. In one 3 officers of the local authority visited the same family: one about the progress of a new baby, another because one of the children was a mongol and the third because the mother minded for gain other children. But none of them was concerned in helping the family as a whole.

It is pointed out that a social worker attached to a group practice is readily available and, therefore used more than if an outside social agency has to be called in.

She should participate in routine or special group discussions on particular patients and families

As time passed the attitude of the doctors to the presence of a social worker as part of the Centre team swung from scepticism about the value of social work to completely unrealistic demands on her resources. It is only now realized that she cannot always find suitable work or a new house for those who need them but " the doctor and social worker must pool their resources and think about their work together in terms of the achievement of reasonable expectations and limited aims ".

[It is clear that the experiment is a success. It would be valuable to have comparable information from Health Centres and Group Practices where similar functions are performed by Health Visitors or other local authority staff.] *Allen Daley*

Vital Statistics and Epidemiology

LOTTE, A. & ROUILLON, A. Mortalité par tuberculose en France en 1955. Répartition par formes cliniques, par âge et sexe, et répartition départementale. [**Mortality from Tuberculosis in France in 1955. Distribution by Clinical Forms, Age and Area**] *Bull. Inst. Nat. Hyg.* Paris. 1957, Jan.–Mar., v. 12, No. 1, 3–30, 11 figs.

Compared with 1954 there was no change in mortality from pulmonary tuberculosis but deaths from tuberculous meningitis fell by one-fifth. The crude death rate of males from the respiratory forms was nearly 3 times the rate of females whereas non-respiratory forms show only a slight excess in the males. The excess of respiratory tuberculosis in males becomes apparent at about age 25. In women the curve rises from childhood up to a peak at age 35, falls slightly up to age 50 and then rises steeply to a peak in old age. In men it rises steeply and continuously from about age 20 onwards to a peak in old age. Respiratory tuberculosis shows a slight seasonal variation with lower rates in the 2nd and 3rd quarters; the other forms have no seasonal variation.

[In considering the variations in mortality with time, age, sex and area it is sobering to note that nearly one-fifth of the total deaths in France in 1955 were ascribed to unknown causes or senility.]

A. Bradford Hill

CRICCHI, L. Mortalità nel commune di l'Aquila nell' ultimo ventennio. [**Mortality Rates in L'Aquila commune in the Last 20 Years**] *Igiene e San. Pubblica.* Rome. 1959, Mar.–Apr., v. 15, No. 2, 144–55.

L'Aquila commune is the most western of the Abruzzi-Molise administrative region, lying in the valley between 2 of the highest mountains of the Central Appenine chain, and the figures given relate to the period 1938 to 1957.

In 1938 the average resident population was 55,465, and in 1957, 57,246. Thus it is evident that though there may have been changes in age distribution (not stated) or through emigration, the total numbers have changed but little. Death rates were 17·03 per 1,000 in 1938, and 10·46 [see note below] in 1957. These rates have followed those for the whole country, but the differences are even more marked because of the high rate for the commune in 1938. Infant mortality rates fell from 135·2 per 1,000 live births in 1938 (for

the province) to 54·2 in 1956 (1957 figures not available).

The two main infectious diseases have been diphtheria and typhoid (not further defined); the 1938 morbidity rates were 217 and 206 per 100,000 respectively and in 1957, 20 and 66. The incidence of typhoid fell abruptly between 1947 and 1948 from never less than 121 cases per year between 1938 and 1947, to never more than 80 cases from 1948 to 1957 with an average of the last 4 years of 40.

The fall in death rates is ascribed chiefly to the fall in infant mortality and in deaths from infectious diseases as the result of improvements in general hygiene, particularly housing and water supplies. The reduction in the infant mortality rate was greatly helped by the beginning of a maternity and child welfare service which included the using of a dried milk powder instead of infected cow's milk. Among the measures against typhoid was the issue of enterovaccine (oral) to the schoolchildren. Anti-diphtheria inoculation has been practised for some time and now any cases that occur are mostly in non-inoculated persons, chiefly adults.

The author speaks proudly of all these achievements, pointing out that no other province of the Region has shown so great an improvement, and also states (perhaps a little too confidently) that there infant mortality has "practically ceased", the remaining infant deaths being due almost exclusively to prematurity (there is apparently a high incidence of twinning) and congenital malformations. The greater degree of general medical and hospital facilities now available have also materially contributed to the good results.

[There are 2 errors in tables 2 and 4. In table 2 the 1957 mortality rate should be 10·46 and *not* 20·46 as printed; in table 4 the morbidity rate should be per 100,000.] *W. K. Dunscombe*

LANCASTER, H. O. **Mortality in Australia, 1951 to 1955.** *Med. J. Australia.* 1959, Mar. 14, v. 1, No. 11, 350–55, 4 figs.

The death rate in Australia during 1951–5 showed a further decline. The death rates were 10·2 per 1,000 for males and 8·2 for females compared with 10·8 and 8·7 in 1946–50. Mortality in infancy and childhood showed a considerable improvement on the rates in the preceding quinquennium for both sexes. The female death rate was lower in each age-group in 1951-5 than in 1946–50, although the improvement in old age was small. Under the age of 15 years the males showed a considerable improvement but at ages 15–19 and 20–24 the rates in 1951–5 were larger than 1946–50, due mainly to accidents, and the death rates at ages over 55 were slightly higher than in the preceding 5-year period. In each age-group the female death rate for all causes was lower than the male rate but for individual causes of death there were a few exceptions. During the reproductive period the cancer death rate was higher for females as a result of cancer of the uterus and breast. The death rates by sex and age and the sex ratio of the death rates are given for the more important causes of death. *W. J. Martin*

BRAVO BECHERELLE, M. A. & REYES JIMÉNEZ, R. Tablas de vida para México de 1893 a 1956. [**Life Tables for Mexico from 1893 to 1956**] *Rev. Inst. Salubridad y Enfermedades Trop.* México. 1958, June, v. 18, No. 2, 81–136, 3 graphs. [20 refs.] English summary (5 lines).

Abridged life tables have been calculated for the United States of Mexico for each calendar year from 1893 to 1910 for both sexes combined and from 1922 to 1956 for the sexes separately. Except for rather more details relating to 1955 and 1956 the presentation is limited to the expectation of life at birth and at intervals from age 1 to age 80. Very little increase in this figure took place at any age between 1893 and 1910 but there was much improvement after 1922. Thus the expectation at birth was 31·70 years for men and 33·46 for women in 1922 and had risen to 55·14 and 57·93 years in 1956. The reduction of infectious diseases in childhood has played an important part. Mortality of women is generally lower than that of men. Similar comparisons are given for each separate state for the 2 years 1930 and 1950. In the latter year the central states have the least favourable position; they suffer, among other hazards, considerable malnutrition. *A. Bradford Hill*

DOUGLAS, C. A. & MCKINLAY, P. L. **Maternal and Infant Mortality in Scotland.** *Health Bull.* (Issued by the Chief M.O., Dept. of Health, Scotland.) 1959, Apr., v. 17, No. 2, 17–44, 6 figs.

This paper, originally prepared for the Scottish Maternity Services Review Committee whose report has recently appeared, is published here after some revision and critical review by the authors. It is a valuable, historical and statistical account of the maternity services in Scotland. With many tables of information and much good analysis and discussion the authors give a clear picture of present maternal and infant mortalities, of the trend in these in the past 30 years or so and of the problems which demand further investigation and research. Examples of the diminution in the mortality rates are: the maternal mortality rate which was 6·38 per 1,000 live births in 1921 was 0·47 (0·03 sepsis) in 1957; infant mortality was reduced from 81·8 per 1,000 in 1931 to 28·6 in 1957.

There is a good summary of the extensive findings. "The outstanding changes in the maternal death rate are, as elsewhere, the practical elimination of mortality from puerperal sepsis and hyperemesis gravidarum which have fallen to only 1 per cent. of their values 25 years ago, a decline to one-tenth in post-abortive sepsis and placenta praevia and to one-six in ectopic pregnancy, accidental haemorrhage, accidents of childbirth, and eclampsia."

"In deaths under 1 month the infectious diseases, acute and chronic, diarrhoea, bronchitis and pneumonia are now numerically infrequent, but little change is observed in congenital malformations and birth injury." "Measurable factors, such as age of mother, parity, social class, and geography, have been examined and their influence on the rates at a given time indicated, but the favourable changes in mortality cannot

be ascribed in any important degree to changes in any of these factors."

Further investigations should be made of morbidity rates for "there seems reason to suggest the extension of statistical appraisal of the effects of reproduction on maternal health to incidence as well as to mortality and perhaps also to surveys at intervals of possible aftermaths". "There remains a vast amount of ignorance" in foetal and neonatal deaths and research into causation particularly of congenital malformations and prematurity is called for. *M. E. Delafield*

MORRISON, S. L., HEADY, J. A. & MORRIS, J. N. **Social and Biological Factors in Infant Mortality. VIII. Mortality in the Post-Neonatal Period.** *Arch. Dis. in Childhood.* 1959, Apr., v. 34, No. 174, 101–14, 9 figs. [25 refs.]

This study was based on almost 1½ million legitimate single births that occurred in England and Wales during 1949 and 1950. The deaths have been analysed by age at death, mother's age, birth rank, social class of father, cause of death and duration of marriage. The still-birth rate increased with the mother's age, and the highest rate was that of the first born. After the age of one week the largest death rate was that of the infants with young mothers, the rate decreased with increasing age of mother but rose slightly for the older mothers, aged 40 +, the rate increased with rank of birth and this trend was apparent in each of the major causes of death. A similar pattern was found in the social classes and geographical regions. Closely spaced children have a higher mortality than other children although spacing (rapidity of breeding), is not the explanation of the phenomenon. Babies of young mothers with 3 or 4 children have an almost equal risk of dying whatever the social class of their fathers. The authors suggest that infection plays an important part in the deaths classified as accidental.

W. J. Martin

THOMPSON, D. J. & CIOCCO, A. **Sickness, Change of Residence, and Death. I. General Results of Follow-Up in Two Population Groups.** *Brit. J. Preventive & Social Med.* 1958, Oct., v. 12, No. 4, 172–82, 1 fig. [10 refs.]

This paper discusses (1) whether persons who complain of some sickness in a household interview, subsequently die or move from the area at a different rate from those who have no such complaint, and (2) to what extent estimates of mortality are affected by the loss from follow-up of those who change their address. These 2 questions are considered for (a) the period 1948–57 in a sample of 2,712 adults first surveyed in Donora, Pennsylvania in 1948 in connexion with the smog episode in that year and (b) the period 1951–6 in a sample of 6,305 adults questioned in 1951 for a morbidity survey.

In both samples the mortality was greater for men than for women and in both sexes increased with age. Change of residence, however, was commoner in the younger groups without any consistent difference between the sexes. In both samples those who reported an illness at the first survey had greater mortality than those reporting no illness, the proportionate difference between the groups being less among older persons. In Donora it was possible to demonstrate that this increase in mortality was the same for those reporting acute illnesses only as for the total group reporting acute or chronic illness. Furthermore the increase was greatest for the few years immediately after survey and became increasingly difficult to demonstrate towards the end of the follow-up period. Subsequent papers will examine which reported illnesses are most closely associated with enhanced mortality. Examination of the data on change of residence, on the other hand, revealed no consistent difference between the groups who were ill and those who were not at the initial survey.

In the Donora study it was shown that those who moved from the city had different mortality from those who stayed. It follows that if complete information on the persons who have moved is not available, estimates of mortality based on the persons remaining in the follow-up will be liable to error. The effect on these estimates of different assumptions regarding mortality within the groups lost to follow-up is discussed in detail. *J. Knowelden*

BENJAMIN, B. **The Measurement of Morbidity.** *J. Inst. of Actuaries.* 1957, v. 83, Pt. 3, No. 365, 225–48. [Numerous refs.] Discussion 249–67.

This is a review of current morbidity measures in Britain by the Chief Civil Statistician at the General Register Office. His discussion is centred on the problem of defining sickness when in many clinical conditions, *e.g.* hypertension, it is impossible to fix a rigid boundary between this state and health. He describes briefly the techniques developed in notification of infectious disease, in tuberculosis, in cancer registration, by the use of insurance and sickness absence records, by personal interview of a random sample of the population, and by the analysis of general and mental hospital records and those of general practitioners. He emphasizes the need for precise definition of all the terms and rates used to describe morbidity, and for a critical assessment of the method employed. He suggests that longitudinal, *i.e.* follow-up studies of healthy persons to observe the emergence of disease among them might add considerably to our knowledge of the value of different measures of morbidity. *J. Knowelden*

Communicable Diseases

For the bacteriology of these diseases see the section on Bacteriology below. For those communicable diseases conventionally regarded as tropical, readers are referred to the TROPICAL DISEASES BULLETIN.

INFECTIVE DISEASES

In this section the abstracts are arranged as far as possible in the following order:—General; Hospital Cross Infection; Diphtheria, Whooping Cough, Streptococcal Infections, Measles, Mumps; Chickenpox; Smallpox; Influenza and other Respiratory Virus Infections, Pneumonia; Hepatitis, Mononucleosis; Meningitis, Poliomyelitis and other Enteric Virus Infections; Arthropod-borne Virus Infections; Enteric Fevers.

BARSY, G. & RUDNAI, O. **The Influence of Age in some Infectious Diseases.** *Acta Microbiologica.* Budapest. 1958, v. 5, No. 1, 59–73, 8 figs.

The age-specific morbidity rates for measles, whooping cough, scarlet fever, diphtheria and poliomyelitis were calculated for Hungary excluding Budapest for 1931–38 and for the whole country for 1949–54. Each disease, except diphtheria, had higher overall rates in the later period, but this may have been partly the result of better reporting. In contrast to the experience of most European countries a shift in age incidence also occurred so that for each disease peak morbidity was in a younger group in the post-war than in the pre-war period. Nevertheless, within each period the trends from year to year of the separate age-specific rates were remarkably parallel, following the pattern of the all ages rate. The authors suggest this is incompatible with the theory that the rise and fall of epidemics is largely determined by the build up and exhaustion of susceptibles; by this theory they would have expected the youngest children without experience of previous epidemics to show greater swings in morbidity from year to year than older groups who had attained some immunity. *J. Knowelden*

WOLF, H. W., HARRIS, M. M. & DYER, W. R. *Staphylococcus aureus* **in Air of an Operating Room.** *J. Amer. Med. Ass.* 1959, Apr. 25, v. 169, No. 17, 1983–7, 4 figs.

Slit-sampler counts of air-borne bacteria were made in a hospital operating room during operations for a period of 9 days. The average number of *Staphylococcus aureus* colonies was about 1 per 100 cu.ft.; from the charts presented the general bacterial count seems to have been between 10 and 20 colonies per cu.ft. On one day a peak count of 23 *Staph. aureus* colonies per 100 cu.ft. (4 colonies collected) was observed. All were type 80/81 and the patient developed post-operative infection with this type. The staphylococcus might, however, have been brought into the room with the patient. *R. E. O. Williams*

YOW, E. M., YOW, Martha D., WOMACK, G. K. SAKUMA, T. & MONZON, Ofelia T. **The Management of Hospital-Acquired Staphylococcal Infections.** *Arch. Intern. Med.* 1958, Dec., v. 102, No. 6, 948–59, 5 figs. [19 refs.]

An epidemic of staphylococcal infections in the Jefferson Davis Hospital, Houston, Texas, in the first 5 months of 1958 included 123 cases among newborn babies, 18 of whom died. There were at least 16 deaths in the 201 older patients. This led to a review of the hospital's routine for controlling infection, to the establishment of a Committee on Infection—regarded as the most important measure—and the institution of regular recording of cases of infection. Among the control measures emphasized are improved care in general hygiene and "housekeeping", isolation of septic patients, treatment of nasal carriers of dangerous staphylococci and reduction in the indiscriminate use of antibiotics. The antibiotics available for treating infections due to "hospital staphylococci" are discussed. *R. E. O. Williams*

VAN GELDER, D. W., CAREY, D., COLVIN, S. H., Jr. & RANDALL, W. S. **Neonatal Infections in a Community Hospital. Report of Two Outbreaks.** *J. Amer. Med. Ass.* 1959, Feb. 7, v. 169, No. 6, 559–66, 3 figs. [13 refs.]

The first outbreak, in 1956, comprised 4 infants, 3 of whom died within 16 days of birth with general sepsis. *Listeria monocytogenes* was isolated from the blood of 1 and the spinal fluid of the 2nd and 3rd (1 of whom survived); haemolytic streptococci were found in the blood of the 4th.

The 1957 outbreak, developing in September and reaching a peak in December, comprised 26 infants. The principal symptoms, mostly developing in the 2nd week of life, were fever, anorexia and irritability; 17 infants had some signs of umbilical sepsis and 12 had infective skin lesions. 9 infants died. Group A streptococci were recovered from several infants, but a variety of other streptococci were also recovered and it does not seem that the microbial aetiology of the outbreak was satisfactorily explained. Some tests were made for Coxsackie virus in faeces, but only late in the disease; no virus was found. It is noted that, at the time of both outbreaks, the nursery was seriously overcrowded. *R. E. O. Williams*

SHAFFER, T. E. **The Problem of Staphylococcal Infections in Infants and Children.** *Ann. Intern. Med.* 1959, Mar., v. 50, No. 3, 614–20. [24 refs.]

Since 1954 Shaffer and his colleagues have examined staphylococci from more than 70 epidemics of staphylococcal disease in maternity unit nurseries; all belonged

to type 80/81. Colonization of infants with the epidemic strain occurs early in life but the lesions may develop later; septic lesions in infants under 3 months and their mothers should therefore be made a reportable disease. In nursery epidemics, carriers have usually been discovered among the staff; in the University Hospital in Columbus, Ohio, monthly surveys are conducted to detect carriers, and staff harbouring "known pathogenic strains" are excluded from the nurseries. In 9 months of this policy, "no clinical infections among infants or mothers have been noted."

In epidemics it is recommended that the epidemic type of staphylococcus should first be determined and any carriers of this type excluded; all infected cases and carriers should be isolated and separate nursery accommodation be opened for newborn babies. In epidemics of high virulence antibiotic prophylaxis may be needed, but should be discontinued as soon as possible.

[Although staphylococci of type 80/81 have recently been the commonest cause of epidemics, they are certainly not the only epidemic type (as shown in a summary of type distributions by the reviewer, this *Bulletin*, 1959, v. 34, 518) and if this is accepted the policy of exclusion of potentially dangerous carriers becomes more difficult.] *R. E. O. Williams*

PAYNE, D. J. H. **Staphylococcal Cystitis in a Gynaecological Ward.** *J. Clin. Path.* 1959, May, v. 12, No. 3, 286–8.

An outbreak of staphylococcal cystitis in a gynaecological ward is described. Between May and November 1955, 37 of 138 patients developed post-operative cystitis; 20 of these were due to a penicillin- and streptomycin-resistant *Staphylococcus aureus* and the 12 strains which were phage-typed belonged to type 7.

Infection was more common after vaginal than abdominal operations. Neither of the surgeons involved carried the epidemic strain and its presence in 2 specimens of urine in the absence of pus suggested that the organism was introduced during catheterization in the ward.

Penicillin-streptomycin pessaries had been used before operation in patients undergoing vaginal operations. Catheterization was performed without gloves, with a lubricated catheter. The lubricant was not thought to be the source of the epidemic staphylococcus.

Although the epidemic strain was present in the noses of 3 ward nurses these cases could not all be attributed to these carriers, and it was present on blankets and in dust from the ward and sterilizing room. The investigation was begun 4 months after the first cases, there had been time for a wide distribution of the organism and it seemed probable that contamination of sterile catheters took place from the blankets and dust at the time of catheterization.

The ward was cleaned; blankets were treated with Lissapol and Cirrasol OD; catheterization was carried out with full aseptic technique without lubricant, and the use of antibiotic pessaries was discontinued. Only 1 case of staphylococcal cystitis occurred after 384 similar operations in the following 17 months.

M. Patricia Jevons

PAULE, W. & CONTE, N. F. **Staphylococcal Septicemia. Report of a Case with Hyponatremia and Eventual Recovery Through Use of Multiple Antibiotics and Adrenal Steroids.** *Arch. Intern. Med.* 1959, May, v. 103, No. 5, 796–8, 2 figs.

"A case report of a 17-year-old youth with staphylococcal septicemia, presumably secondary to bronchopneumonia, is presented, with eventual recovery following use of multiple antibiotics and adrenal steroids. The hyponatremic state, unresponsive to massive salt replacement but dramatically corrected with hydrocortisone, is the interesting and outstanding feature."

TASMAN, A. Het verband tussen de aard van de gebruikte entstof, de wijze van inspuiten en de entreacties na immunisatie tegen kinkhoest, difterie en tetanus. [**Relationship of Type of Vaccine and Method of Inoculation to Vaccination Reactions after Immunization against Whooping Cough, Diphtheria and Tetanus**] *Nederl. Tijdschr. v. Geneesk.* 1959, May 16, v. 103, No. 20, 1049–57, 4 figs.

"A study was made of the relationship of the type of vaccine and method of inoculation to the reactions following immunization against whooping cough, diphtheria and tetanus. Among 432 children, 620 inoculations comprised one inoculation in 275 children, two in 126 and three in 31 children. The results were examined after 1 day, 3 days, 8 days, 1 month and 2 months.

"It was observed that the number, nature and duration of the reactions, chiefly local ones, depended on the method of injection: considerably more reactions of longer duration were seen after subcutaneous injections than after intramuscular injection of the vaccine. The type of vaccine used was also found to be of marked influence. Multiple antigens containing pertussis vaccine (pertussis-diphtheria-tetanus and pertussis-diphtheria) caused considerably more reactions, whatever the method of injection, than those without the pertussis component (diphtheria, tetanus and diphtheria-tetanus). There was no evidence that the sex of the (mostly very young) children had any influence on the number of reactions. As regards the children's ages, there seems to be an indication, although not a statistically significant one in view of the 95 per cent. reliability interval, that older children have a stronger reaction to antigen injections than young ones.

"Generally speaking, inoculations performed before we started our investigation appeared to be of little consequence in later reactions. Two or three injections given in the course of the investigation produced a slightly stronger reaction than a single inoculation, except when performed in a combination of subcutaneous inoculation (first time) with intramuscular inoculation (second time), and intramuscular (first and second time). The latter combination yielded considerably fewer positive reactions after the second (intramuscular) injection than the former.

"Some practical consequences of these results are discussed."

SPILLER, Violet, GROARKE, F. L., BARNES, Joan M. & HOLT, L. B. **Diphtheria Prophylaxis. Long-Term Efficiency of Separate and Combined Antigens administered Early in Life.** *Brit. Med. J.* 1959, Jan. 10, 96–7.

The authors compared results in infants inoculated from 3 months onwards with (a) 3 doses of *Haemophilus pertussis* vaccine followed by 2 0·5 ml. doses of PTAP, (b) 3 doses of combined fluid diphtheria toxoid and *H. pertussis vaccine* [this *Bulletin*, 1956, v. 31 363]. Both methods gave excellent results with serum antitoxin titres of 0·112–0·131 unit/ml. 4½ years later.

After an interval of one year, however, a higher average titre was observed in the children who had been immunized by the first method. *J. W. McLeod*

THORBURN, W. B. **Schick Test Results in R.A.F. Boy Entrants.** *Pub. Health.* 1958, Dec., v. 73, No. 3, 103–8.

From June 1957 to June 1958, 1,824 boy entrants to the R.A.F. were Schick tested, the intradermal injections being given by one of 5 medical officers while all the results were read at 48 hours and 7 days by one doctor. The proportion of susceptibles thus revealed was 31%, very close to the 29% found in a previous study of adult recruits [this *Bulletin*, 1958, v. 33, 205]. The 2 studies differed, however, in the proportion of positives and weak positives among the susceptibles; among recruits there were 22% positive and 6% weakly positive of the sample examined compared with corresponding proportions of 10% and 21% in the boy entrants. This difference is unlikely to be due to differences in exposure to diphtheria. It might have occurred because the recruits were born before the war and had reached school age before the immunization campaign was well established so that, as a result, many would have very low levels of circulating antitoxin; the boy entrants on the other hand were born in the years 1941–3 and would have had greater opportunities for primary and reinforcing immunization.

Although no differences were found between the proportion of positives in those born in the separate years 1941, 1942 and 1943, an analysis by area of residence showed that the highest proportions were in entrants from Ireland, Wales and the Northern Counties, 39%, and the lowest in those from the Great Towns, 24%, and from Scotland, 23%. The samples are too small for these area rates to be precise. No significant difference was found between the results of tests performed by the 5 operators, and it is concluded that Schick testing is worth while and suitable for general application in the Service. *J. Knowelden*

OLITZKI, Z. **Epidemiological Observations on Diphtherial Infections in Jerusalem. I. Results obtained from Laboratory Reports of the Rothschild Hadassah-University Hospital 1920–1956.** *Acta Med. Orientalia.* 1957, Mar.–Apr., v. 16, Nos. 3/4, 72–86.

In this period of 37 years just over 2,000 cases of diphtheria were diagnosed in one of the 3 main laboratories in Jerusalem. There were 2 periods of unusually high incidence, 1935–41 and 1951–4. All types of infection were commonest in the autumn and early winter months. The site of infection was the pharynx in 36%, the nose in 41%, the skin in 9% and the ear in 12%. The relatively high proportions of nasal and aural types were probably due to the activities of ENT and welfare clinics which provided many of the specimens. Pharyngeal infections were rare in the first 6 months of life, but otherwise the chief features of the age-distribution were the preponderance of nasal infection in children of 6–14 years, and of pharyngeal infection in adults. The Oriental Jewish patients from whom *Corynebacterium diphtheriae* was isolated were younger than the Ashkenazim patients, and had a smaller proportion of pharyngeal infections. In this study pharyngeal carriage was observed for 3 months and from other sites the organism was recovered for a period of over 6 months. The average duration of the carrier state was least for infections starting in the July–September quarter. In families with multiple infections the primary case was commonly nasal but gave rise on occasions to secondary cases at other sites. *J. Knowelden*

AGNESE, G. Sulle oscillazioni stagionali della frequenza dei portatori di C. diphteriae. **[Seasonal Fluctuations in *C. diphtheriae* Carrier Rates]** *Igiene Moderna.* 1958, Nov.–Dec., v. 51, Nos. 11/12, 859–66, 1 graph. English summary.

The diphtheria carrier rate was studied in 11,530 children between 3 and 14 years admitted to an institution in Pietra Ligure, near Savona, between 1951 and 1956; all the children came from the Milan area. The study which consisted in a harmonic analysis of the seasonal changes in the carrier rate frequencies showed (1) that there were constant differences in the monthly carrier rates, with the higher values between October and March, and (2) that the only important wave was the fundamental one of a 12-month period with a maximum in December. The morbidity and carrier rate incidence curves were virtually superimposable. The hypotheses that the 12-month curve denotes changes in the frequency of opportunities for infection and that a 6-month curve indicates variations in receptivity were borne out. *E. Agius*

MITEL'MAN, S. L. **Efficacy of Active Immunization against Scarlet Fever by Depot Preparations.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, No. 9, 1349–55. [Translated from Russian.]

The author first reviews briefly a number of studies made over several years of the value of purified precipitated scarlet fever toxin. 3 injections seemed insufficient to induce solid immunity, as judged by Dick tests, and even with revaccination later some children reacted to 4 or 10 skin test doses. Nevertheless when tested 24 months after the beginning of vaccination, the vaccinated children had a clear advantage, in Dick tests, over unvaccinated; and only 0·4% of them had had scarlet fever, compared with 15·9% of the control

group. [Neither the method of selection of the controls nor the method of ascertainment of the disease, is stated.] *R. E. O. Williams*

PARTINGTON, M. W. & QUINTON, J. F. P. **The Pre-Eruptive Illness of Measles.** *Arch. Dis. in Childhood.* 1959, Apr., v. 34, No. 174, 149–53, 2 figs. [23 refs.]

This is a study of the onset of measles based on a review of records of 82 cases of measles occurring in hospitals in Norwich between 1951 and 1958. The authors find that in 57 the prodromal illness lasted 7 days or less but in the remaining 25 from 8 to 16 days. Of these 25 patients, 17 had a continuous illness from the presumed date of infection to the rash, the other 8 had a biphasic type of illness, the first phase coinciding perhaps with viraemia immediately after infection—the illness of infection—the second phase with a second and more severe viraemia after an incubation period.
A. B. Christie

CONDON, F. J. **Erythema Infectiosum—Report of an Area-Wide Outbreak.** *Amer. J. Pub. Health.* 1959, Apr., v. 49, No. 4, 528–35. [15 refs.]

This is an account of an outbreak of erythema infectiosum occurring in the Detroit Metropolitan area in 1956 and 1957. The first cases were probably diagnosed as measles, rubella or scarlet fever but it soon became apparent that a disease different from any of these was spreading in the community. The incubation period appeared to be between 4 and 14 days and the disease spread in homes and school classes. It affected mainly children but adults did not escape and tended to be more ill than the children. Prodromal symptoms were mild and often missed. The rash first appeared as a bright erythema on the face, often with marked circumoral pallor, and sometimes with butterfly pattern across the bridge of the nose. Within 1 to 4 days the rash appears on the extensor aspects of arms, thighs and legs stopping short at the wrist and ankles: the rash now tends to be more macular especially distally: it may spread to neck and trunk but is not heavy there. In the third stage the rash disappears and recurs repeatedly and this feature may persist for days or weeks. Occasionally purpuric rashes may occur. The disease is always mild but malaise and fatigue may last for a considerable time. It is important to differentiate the condition from others, especially measles, which may be more severe. Exclusion for one week of all patients suffering from an exanthematous disease was practised in order to avoid such mistakes. No laboratory investigations to search for a virus were carried out. [This is a valuable description of the disease and well worth reading in the original.]
A. B. Christie

SCARABICCHI, S. & JANNUZZI, C. Due casi di embriopatia rubeolica. [**Two Cases of Embryonic Defects as a Result of Maternal Rubella**] *Giorn. di Malattie Infettive e Parassit.* 1959, Apr., v. 11, No. 4, 284–8, 7 figs. [28 refs.]

SCHREUS, H. T. & HEINISCH, E. Megalerythema epidemicum. II. Mitteilung. [**Erythema infectiosum II**] *Schweiz. med. Woch.* 1959, May 30, v. 89, No. 22, 584–90, 7 figs. [58 refs.]

In a previous paper [this *Bulletin*, 1959, v. 34, 313] there was a preliminary account of the recent widespread epidemic of erythema infectiosum (also known as megalerythema epidemicum, *Ringelröteln* and by other names) in Germany in 1958. In the present paper the disease is described in considerable detail. There is a long historical account, based on many references, of the experience of erythema infectiosum or of diseases which were similar to this infection, since the eighteenth century, with a list of reported epidemics in the continent of Europe and elsewhere since 1910. Some account is also given of reported work on the aetiology of the infection.

The authors had personal experience of 79 cases of the disease in Western Germany during the epidemic. These cases are described in considerable clinical detail with photographs of the macroscopic and microscopic appearances of the skin lesions. The findings of blood examination and the results of some complement-fixation tests with different virus strains are also recorded.

It is noted that there were certain differences between the observations made in these cases and those recorded in former epidemics. These differences are: extensive geographical spread of the disease, high general incidence, age incidence highest in adults, more cases in adult females than in men and children, the presence of itching, occasional high fever and oedema, vesicles on the extremities which were sometimes confluent, exanthemata on the palms of the hands and the soles of the feet, leucocytosis of 7,000 to 26,000 and eosinophilia between 5% and up to 24%. *M. E. Delafield*

MASLENNIKOVA, L. K. **The Skin Test in Epidemic Parotitis.** *Problems of Virology.* London. 1958, v. 3, No. 2, 85–9, 2 figs. [Translated from Russian.]

A skin test antigen was prepared by ultraviolet inactivation of amniotic fluid containing mumps virus with a haemagglutinin titre of 128; an area of erythema of 15 mm. or greater in diameter 24 hours after intradermal injection was regarded as a positive result. In 239 children and adults suffering from mumps a positive reaction was obtained in 22% of 40 tested on the 2nd–3rd day of illness, 50% of 56 tested on the 4th–5th day and in 78% of 51 tested on the 8th–9th day. The test was also positive in 54 of 63 (85·7%) healthy persons who had previously suffered from the disease and in 63 of 220 (28·6%) who stated that they had never had mumps. *D. J. Bauer*

UTZ, J. P., SZWED, C. F. & KASEL, J. A. **Clinical and Laboratory Studies of Mumps II. Detection and Duration of Excretion of Virus in Urine.** *Proc. Soc. Exper. Biol. & Med.* 1958, Oct., v. 99, No. 1, 259–61.

65 specimens of urine from 13 patients suffering from mumps were subjected to ultracentrifugation and

the sediments were resuspended in saline to 1/10 of the original volume and inoculated into HeLa and monkey kidney cell cultures. Mumps virus was recovered in this manner from all the patients; it was found in 70% of specimens taken during the first 9 days of illness and in 55% during the first 14 days. 57 specimens were also prepared for inoculation by simple dilution, but virus was isolated less frequently than by the concentration method.

[For Part I, see this *Bulletin*, 1958, v. 33, 96.]

D. J. Bauer

KLIACHKO, N. S., GUSARSKAIA, I. L., MASLENNIKOVA, L. K., SENA, N. L. & TSIRLINA, S. S. **The Specific Prophylaxis of Epidemic Parotitis—IV. The Study of the Epidemiological Effectiveness of Intradermal Vaccination with Live Attenuated Parotitis Vaccine in Institutionalized Groups of Children.** *Problems of Virology.* London. 1958, v. 3, No. 1, 25–31, 3 figs. [19 refs.] [Translated from Russian.]

In 1955–6 4,174 children aged 3–6 years attending 160 kindergartens in Leningrad were given a single dose of live mumps vaccine by intradermal inoculation and 5,584 children belonging to the same groups were left unvaccinated. Slight or moderate general reactions were observed in 16 instances (0·38%). During subsequent observation for 2½ to 5 months cases of mumps occurred in 60 kindergartens; of 2,390 unvaccinated children who had not had mumps previously and were exposed to infection 196 (8·2%) developed mumps, compared with 16 of 1,735 vaccinated children (0·92%).

D. J. Bauer

LAUTROP, H., HOLM, P., ANDERSEN, E. K., SCHEIBEL, I. & TULINIUS, S. Orientering om vaccination mod kighoste. [**Comments on Vaccination against Whooping-Cough**] *Ugeskr. f. Laeger.* 1959, May, 21, v. 121, No. 21, 819–24.

The State Serum Institute in Copenhagen is still engaged in the production of a triple vaccine (against diphtheria, tetanus and whooping-cough) not yet issued for general use. It is hoped that in the course of 1959 tests will have been completed with a view to ascertaining the frequency and severity of its side-effects. A member of the Institute's staff, Else Krag Andersen, has embodied 10 earlier publications and much other, hitherto unpublished information on whooping-cough vaccination in a volume which she successfully defended for the Pharmaceutical Doctorate early in 1959. The present study, to which she has contributed with 4 of her colleagues, is a plea for early prophylactic vaccination with a whooping-cough vaccine by itself, therapeutic vaccination with it being of dubious value though it may be tried early in the disease at a time when prophylactic vaccination has not been well established.

The first table deals with the notifications of and deaths from whooping-cough in Denmark between 1930 and 1957, and the second with the deaths from this disease between 1950 and 1957. Though the number of these deaths has fallen greatly during the past 30 years, they still amount to some 25 yearly, with about 75% of them under the age of 1 year. Hence the advice that prophylactic vaccination should be started soon after birth. The first injection should be given at the age of 5 weeks, the second a month later, the third after another month. A fourth injection should be given after about a year. With this procedure it should be possible to confer a certain degree of immunity during the dangerous first 2 years of life, and to render infections less severe later in life. Considering the mild course run by parapertussis, it should not be necessary to vaccinate against it, and parapertussis organisms have therefore not entered into the composition of this whooping-cough vaccine.

Claude Lillingston

NICHOLS, W. W. **Experiences with Chickenpox in Patients with Hematologic Disease receiving Cortisone.** *J. Dis. Children.* Chicago. 1957, Sept., v. 94, No. 3, 219–23, 5 figs. [21 refs.]

3 boys, aged 3, 2¾ and 5 years were being treated with cortisone for blood diseases when they contracted chickenpox. The first 2, who were receiving the equivalent of 100 mgm. and 75 mgm. cortisone daily, died apparently from severe chickenpox. The third was receiving 100 mgm. daily but this was at once reduced to 25 mgm. daily: the chickenpox was mild and the child recovered. The author refers to another patient on high cortisone dosage who developed measles and died and to 3 others on lower dosage who recovered from measles. He suggests that for children on cortisone treatment who develop chickenpox or measles the dosage should be reduced and chickenpox convalescent serum, or, for measles, gamma globulin should be given. He refers to the possibility of the activation of tuberculosis by cortisone and suggest that children having cortisone for leukaemia should as a routine be given prophylactic isoniazid and streptomycin therapy.

A. B. Christie

CHASSAGNE, P. & VIGUIÉ. Situation épidémiologique en France en 1955. [**Epidemiological Situation in France in 1955**] *Rev. d'Hyg. et de Méd. Sociale.* 1958, July–Aug., v. 6, No. 5, 469–503, 21 figs.

The outstanding feature of the infectious disease experience of France in 1955 was an epidemic of smallpox, the worst in 30 years [descriptions are given in this *Bulletin*, 1956, v. 31, 365, 794].

The epidemic illustrates several features which may be relevant to the situation in Britain as well:—

(i) Early diagnosis is rare because few doctors have seen smallpox.

(ii) Populations which are inadequately vaccinated, as in Brittany, are particularly at risk of epidemics on the introduction of infection from abroad. North Africa, where mass vaccination is practised, provides far less of a hazard than the Far East.

(iii) The decline of infectious disease has led to the reduction of infectious disease units, which are then incapable of meeting such an emergency.

(iv) Mass vaccination is rarely followed by complications. Despite a 5-fold increase, to nearly 6 million

vaccinations and revaccinations in 1955 compared with 1,200,000 in the previous year, the reported deaths from encephalitis [presumably from all causes] in the first half of these years fell from 140 to 118.

By comparison with smallpox, other infectious diseases presented much the same picture as in 1954. The enteric fevers had reached the lowest recorded levels in 1954 with just under 4,000 reported cases and 105 deaths, but in 1955 there was a slight rise to 4,537 cases with 124 deaths. In the same year Britain had just over 1,000 cases. The highest incidence rates were in boys 10–14 years and in girls under 10 years. The peak of the epidemic was in September.

Poliomyelitis presented a similar picture with a small increase over the previous year, 1,834 cases compared with 1,534 with corresponding rates of 4·2 and 3·5 per 100,000. Whooping cough notifications rose from 6,110 in 1954 to 6,738 in 1955. This disease is grossly under-reported; in Britain, where notification is probably incomplete, 79,000 cases were reported in 1955. On the other hand in France there were 388 deaths in 1955 compared with only 88 in Britain. Whooping cough vaccination is not widely practised in France.

Measles is also under-reported. In 1955, a year of low incidence, there were 14,916 reported cases compared with 36,643 in the previous year; in Britain nearly 700,000 cases were reported in 1955.

Diphtheria morbidity was the lowest on record with 2,155 reported cases. The persistence of this disease in some areas is blamed on inadequate immunization, fostered by vigorous anti-vaccination campaigns.

Brucellosis cases had declined from 967 in 1954 to 697 in 1955. Peak morbidity was between 25 and 40 years of age and 80% of cases were in men. The Mediterranean and Alpine regions continue to be the main centres of infection. Meningococcal meningitis and scarlet fever notifications had also declined. Deaths from tetanus, 449, exceeded the number of cases notified, 431, and there was a reduction from 50 to 26 in infant deaths from this cause.

4 cases of tularaemia, 51 of leptospirosis and 4 of rickettsial infection were reported. 2 of the 3 patients with *Rickettsia prowazeki* had relapses of old infections, and the third was in an American visitor. Food poisoning was increasingly reported, and included episodes due to staphylococci and salmonellae.

J. Knowelden

World Health Organization. Technical Report Ser. No. 170. **Expert Committee on Respiratory Virus Diseases. First Report, Stockholm, 11–15 August 1958.** 59 pp., 1 fig. [Numerous refs.] 1959. Geneva: Palais des Nations. [Sales agent for U.K., H.M. Stationery Office.] [3s. 6d.; $0.60; Sw.fr. 2.–.]

A great deal of valuable information on respiratory virus infections is contained in this report. The respiratory syndromes of viral aetiology are divided into 4 groups represented by (1) influenza, (2) common cold, (3) atypical or virus pneumonia and (4) unclassified acute respiratory disease (febrile catarrh). The fourth group is subdivided into (a) acute respiratory disease, (b) non-bacterial exudative pharyngitis, (c) pharyngo-conjunctival fever, (d) kerato-conjunctivitis, (e) obstructive laryngo-tracheo-bronchitis of infants or croup and (f) acute pneumonitis. The association of each of these syndromes with known viruses is discussed.

Influenza viruses are divided into types, A. B and C. Type A viruses are divided into 3 sub-groups or families, the first (sub-group A) including A viruses predominant up to 1946, the second (sub-group A1), formerly referred to as A-prime and representing the viruses predominant from 1946 to 1957, and the third (sub-group A2) represented by the Asian strains. The evolution and possible mechanisms for antigenic variation among influenza viruses are discussed. Epidemiological aspects of the 1957 influenza pandemic are presented and the possible relationship between animal and human influenza is considered. The pathology, prophylaxis and treatment of influenza are discussed and recommendations regarding control measures against severe epidemics of influenza are reviewed. The importance of the cooperation between laboratories in many countries participating in the WHO influenza programme is very clearly brought out and the extension of this programme to other respiratory diseases is recommended. Developments in laboratory techniques used in the study of influenza are brought up to date and detailed descriptions of serological and diagnostic techniques are annexed to the report.

Adenovirus infections are reviewed with reference to aetiology, clinical syndromes, epidemiology, laboratory diagnosis and prophylaxis.

Attention is also given to miscellaneous respiratory viruses comprising non-influenzal myxoviruses (Sendai virus, haemadsorption viruses (types 1 and 2 and croup-associated or acute laryngo tracheo-bronchitis virus), respiratory syncytial virus (CCA and Long strains), atypical pneumonia virus (Eaton's agent), JH and 2,060 viruses, psittacosis and Q fever, common cold and entero-viruses. It is suggested that a useful contribution by WHO would be to help in arranging for the study, comparison and distribution of newly-isolated respiratory viruses.

H. G. Pereira

Holland, W. W., McDonald, J. C. & Wilson, J. S. **Asian Influenza in the Royal Air Force in the United Kingdom, 1957–58.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1959, Apr., v. 18, 65–70, 2 figs.

The 1958 outbreak of Asian influenza in the Royal Air Force in Great Britain began at the end of August and the beginning of September in the boys and recruits centres and the attack rate from acute respiratory diseases rose rapidly to a maximum of about 220 per 1,000 and Asian influenza continued to cause a high rate of sickness during the rest of the winter in these centres. Asian influenza appeared a little later in the operational units and acute respiratory diseases reached a maximum attack rate of 120 per 1,000 in October and then declined and only sporadic cases of Asian influenza were recorded in the remainder of the winter. For all units the recorded incidence of influenza in the

5 months August to December was 0·4, 7·2, 10·1, 2·9 and 1·3%. The incidence of acute respiratory diseases during August to November varied from 18 to 30% in the different regions of the country. Serological tests were carried out in one of the recruit centres and the findings suggest that only one-third of those attacked were ill enough to be admitted to hospital; this implies that the infection rate was probably well over 40%. No second attacks were confirmed and in the period December to April almost all the illness confirmed as influenza A was in persons who said that they had not been ill during the autumn epidemic.

W. J. Martin

FRASER, P. K., HATCH, L. A., SHELL, G. N. & FORSTER, Jill M. R. **Influenza C in a Naval Recruit Population.** *Lancet.* 1959, June 20, 1259–60.

"Sera were obtained from 439 boys on the day they joined a training establishment and again three months later.

"68 showed significant rises in complement-fixing antibody titres to influenza virus C, and 6 of these also had rises against other viruses.

"Less than half those who had influenza C were sufficiently ill to seek medical advice."

HENNESSEN, W. & COLLI, A. Epidemiologische und serologische Beobachtungen bei der Influenza-Pandemie 1957. [**Epidemiological and Serological Observations during the Influenza Pandemic of 1957**] *Ztschr. f. Hyg. u. Infektionskr.* 1958, v. 145, No. 3, 221–7, 4 figs. [13 refs.]

Complications involving the central nervous system occurred in 8·6% of 755 patients with Asian influenza observed by the authors in Germany in 1957/58 compared with 0·5% of 471 patients during the influenza pandemic of 1918; fatal cases amounted to 0·3% and 21·9% for the 2 periods respectively. The first cases in West Germany occurred in September. The curve of age-incidence was biphasic, with maxima of 16% and 7% at 15–20 and 55–60 years respectively, separated by a minimum of 3–4% at 40 years, comprising persons who were infants at the time of the 1918 pandemic. Complement-fixing antibody to the FM1 strain was found in all of 62 sera taken from patients during the epidemic, and to A/Asia/57 antigen in 52 sera (83·9%); the former antigen gave higher titres and was of greater value for diagnostic purposes than the prevalent strain.

D. J. Bauer

SPRÖSSIG, M. Erfahrungen mit der Mikrokomplement-bindungsreaktion während der Grippeepidemie 1957. [**Experiences with the Microcomplement-Fixation Test during the Influenza Epidemic of 1957**] *Ztschr. f. Hyg. u. Infektionskr.* 1958, v. 145, No. 3, 228–34, 3 figs. [11 refs.]

The microcomplement-fixation test with V antigen in the form of crude allantoic fluid has been used in investigations of the 1957 epidemic of Asian influenza in the Jena area. Strains of influenza virus were isolated from 3 patients and were identified as Asian strains by ISAACS. In an investigation of paired sera from these patients haemagglutination-inhibition tests with A/Singapore 6/57 antigen a positive result was obtained in 1 instance only, whereas the complement-fixation test gave a positive result in all 3 patients. The acute-phase sera all showed a higher titre of A-prime (FM1) complement-fixing antibody than that of a pool of sera obtained before the epidemic, and in the examination of 618 acute-phase single sera taken during the epidemic it was possible to make a diagnosis of Asian influenza on the basis of a rise in A-prime complement-fixing antibody in 70% of instances, whereas tests with A/Singapore 6/57 antigen gave positive results in only 39%.

D. J. Bauer

ALTEVOGT, R. Nachweis komplementbindender Antikörper bei Influenza. [**The Detection of Complement-Fixing Antibodies in Influenza**] *Arch. f. Hyg. u. Bakt.* 1958, Oct., v. 142, No. 7, 535–9. [10 refs.]

Complement-fixation tests with PR8, FM1 and A/Asia/57 antigens have been carried out in parallel by the tube method of Kolmer and Boerner and by Hennessen's micromodification of the plate method of Fulton and Dumbell on 500 sera from patients with a clinical diagnosis of influenza. Positive results with A/Asia/57 antigen were obtained in 219 instances (43·8%) by the tube test and in 313 instances (62·6%) by the micromethod. With PR8 antigen the figures were 87 (17·4%) and 138 (27·6%), and for FM1 antigen 272 (54·4%) and 315 (63%), for the tube test and micromethod respectively. The micromethod, in which serial dilutions of complement and fixed amount of serum are used, thus appeared to be more sensitive.

D. J. Bauer

VIVELL, O., SCHRÖPL, F., REIMOLD, G. & RICHTER, S. Die Häufungen von Grippe- und Adenovirusinfektionen in Südwestdeutschland im Jahre 1957. Ergebnisse serologischer und klinischer Studien. [**The Incidence of Influenza and Adenovirus Infections in Southwest Germany in 1957. Results of Serological and Clinical Studies**] *Deut. med. Woch.* 1959, Mar. 13, v. 84, No. 11, 510–16, 535–6, 9 figs. [35 refs.]

In 1957 serological investigations for the presence of influenza and adenovirus antibody were carried out in Freiburg, Germany, on 433 sera from 257 patients suffering from acute respiratory infection. An increase in the frequency of adenovirus antibody occurred in winter and spring, and influenza antibody to type B and A/Asia/57 increased in October and November, at the time when the epidemic of Asian influenza reached the area. The results of the serological investigations are discussed in relation to age-group and type of clinical course.

D. J. Bauer

Sohier, R., Thivolet, J., Freydier, J. & Challut-Thal, F. Réactions de fixation du complément chez les sujets atteints de grippe asiatique et role de l'age dans l'élaboration des anticorps réagissant avec différents antigènes du groupe A. [**Complement-Fixation Reactions in Asian Influenza and Influence of Age on the Production of Antibodies to different Group A Antigens**] *Ann. Inst. Pasteur.* 1959, May, v. 96, No. 5, 512–23. [17 refs.]

Results of serological tests performed on 80 sera from patients with Asian influenza are reported. Each serum was tested by complement fixation against soluble A/PR8, soluble A/Formosa/313/57 and viral A/Formosa/313/57 antigens. All sera gave positive reactions with the viral A/Formosa/313/57 antigen but a proportion of negative results was obtained with the soluble antigens. This discrepancy was particularly marked when viral A/Formosa/313/57 and soluble A/PR8 antigens were compared, and it was related to age of the patient, being maximal (26 out of 29 sera) in infants aged 0 to 36 months and minimal (4 out of 16 sera) in patients between 21 and 50 years. Discrepancies between results obtained with viral and soluble Asian antigens were less frequent but similarly related to age of the patients.

It is suggested that the higher reactivity of adult sera with soluble antigens may be due to preceding experience with different strains of influenza A virus.

H. G. Pereira

Gresser, I. & Halstead, S. B. **Serologic Response to Far East Influenza.** *Arch. Intern. Med.* 1959, Apr., v. 103, No. 4, 590–92, 1 fig. [14 refs.]

The value of complement-fixation and haemagglutination-inhibition tests for the diagnosis of Asian influenza was investigated by testing acute and convalescent sera from 271 military personnel suffering from influenza between April and August 1957, and from 23 young adults bled repeatedly after an attack of influenza during the autumn of the same year. Serological confirmation of the clinical diagnosis was obtained more frequently by complement fixation than by haemagglutination-inhibition. Rises in complement-fixing antibodies occurred by the second week of illness, while 3 weeks were required for comparable rises to be revealed by haemagglutination-inhibition. *H. G. Pereira*

Schoenfeld, E., Spigland, I., Jasinska-Klinberg, W. Elazar, M. & Goldblum, N. [**A Clinical and Laboratory Study on Viral Respiratory Infections of Children**] *Harefuah.* Jerusalem. 1959, May 1, v. 56, No. 9 [in Hebrew 227–30 [19 refs.] English summary 230–31].

The English summary appended to the paper is as follows:—

"A study on the viral etiology of respiratory infections in children was undertaken during the winter of 1957/58. 152 infants and children, aged 6 weeks to 13 years were included in this investigation. The children were hospitalized in the Government Hospital, Jaffa and the laboratory tests were carried out in the Virus Laboratory of the Ministry of Health. The clinical material included: cases of pneumonia, spastic bronchitis (bronchiolitis), laryngo-tracheitis and other upper respiratory infections. The laboratory tests consisted mainly of complement fixation (CF) reactions using the antigens to Adenovirus, Q fever, Psittacosis, and Influenza A virus. The CF tests were carried out on paired blood samples, one from the acute phase and the other from the convalescent stage—2 weeks to 3 months after the onset of the disease. No attempts were made to isolate the etiological agents. The overall positive results for all four antigens amounted to approximately 40 per cent. 29 per cent of all the cases were positive showing a four-fold or higher rise in antibody titer, and the rest were presumptive cases (high titer of adenovirus antibody in both the acute-phase and convalescent blood samples). None of the cases was positive for Psittacosis. Positives for Q fever and Influenza A were few. Analysis of the serological results shows that positives for adenovirus were mainly among infants and young children, 6 months to 4 years of age. Influenza positive cases, on the other hand, concentrated in older children—4½ to 13 years old. An analysis of the correlation between the serological results and the various clinical findings is also presented."

Mickerson, J. N. **Influenzal Pituitary Depression.** *Lancet.* 1959, May 30, 1118–21. [23 refs.]

"In each of 4 patients with influenza a similar pattern of symptoms, consisting of fatigue, muscular weakness, severe dyspnœa, aching limbs, and mental depression associated with a low blood-pressure, suggested adrenocortical insufficiency.

"Determination of serum-electrolyte and urinary-steroid excretion levels supported this view, but correction of hyponatræmia and increased urinary steroid excretion following corticotrophin administration indicated that adrenocortical insufficiency was secondary to reduced anterior-pituitary activity.

"Rapid improvement occurred in each patient during administration of corticotrophin and later of prednisolone. In one patient severe mental depression and electro-encephalographic abnormalities disappeared following steroid therapy."

Orford Smith, E. S. & Clements, Daphne I. **Clinical Evaluation of Asiatic Influenza Vaccine in Alberta.** *Canadian J. Pub. Health.* 1959, May, v. 50, No. 5, 179–82.

A clinical trial of an Asian influenza vaccine was carried out in the Provincial Mental Institute, Edmonton, Alberta. A subcutaneous injection of 1 cc. of Asian influenza vaccine was given to 519 patients and a subcutaneous injection of 1 cc. of a placebo was given to 516 patients. The patients were selected at random and the substances used were of a similar physical appearance. Among the patients receiving the Asian vaccine the incidence of influenza-like illness was 5·8%, and 14·5% among the controls. The difference of 8·7% was significant and indicates a protection

rate of 60%. The staff were inoculated about one week after the patients but, because of limited supply, they only had an intradermal dose of 0·1 cc. of Asian vaccine, from another source. The influenza attack rate among the 318 staff vaccinated was 42·1%, being 3 times the attack rate of the controls and 7 times the rate of the group of patients receiving vaccine. [The relative position of the 3 groups was unchanged if the attacks of influenza occurring in the first week after inoculation are omitted.] The different procedure invalidates any comparison of staff and patients but it is probable that the staff were at greater risk of contracting infection. *W. J. Martin*

FUKUMI, H., NISHIKAWA, F., KURIMOTO, U., INOUE, H., USUI, J. & HIRAYAMA, T. **Epidemiological Studies of an Outbreak of Epidemic Keratoconjunctivitis in Ogaki City and its Vicinity, Gifu Prefecture in 1957.** *Japanese J. Med. Sci. & Biol.* 1958, Dec., v. 11, No. 6, 467–81, 3 figs. [11 refs.]

An epidemic of keratoconjunctivitis occurring mainly among school children and their family contacts is described. The attack rate reached a peak in early September 1957 and varied from 0·2 to 20·9% in 16 schools included in the investigation. The epidemic was preceded by sporadic cases reported during the 2 previous months. Evidence is presented suggesting that the use of swimming pools may have contributed to the spread of infection. The incubation period, estimated from the dates of onset of disease among household contacts, varied from 5 to 14 days.

6 strains of adenovirus type 8 were isolated from conjunctival scrapings collected from 9 patients. Virus isolations were carried out in HeLa cell cultures which showed cytopathic effects typical of adenovirus type 8 starting from 13 to 22 days after inoculation of the cultures. Acute and convalescent sera from 13 patients were tested for neutralizing antibodies against adenovirus type 8 and showed relatively small rises in titres in all but 2 cases. *H. G. Pereira*

STENSTRÖM, R. **Pneumonia in Adults during the Influenza Epidemic of 1957. Roentgenological Observations.** *Ann. Med. Intern. Fenniae.* Helsinki. 1959, v. 48, Suppl. 28, 243–51, 4 figs. [11 refs.]

158 adult patients with pneumonia admitted to hospital in October–November 1957 are classified: 30% had severe forms and there was a shift to the older age-groups. There were 15 deaths, 11 being in patients with concurrent diseases. In 6 of 13 autopsies, pulmonary abscesses were found. The predominating organism was *Staphylococcus aureus* (34% incidence in severe cases). Double pneumonia was present in almost 50%, as was also atelectasis; evidence of pleural irritation was found in 75%. Abscesses, empyemas and spontaneous pneumothorax were more frequent than in control cases, and bronchiectasis was diagnosed in 11%.

Asian influenza seemed to be more severe than usual in this district, and the severity of the pneumonia compared unfavourably with that of the epidemic of 1953–4. *H. Stanley Banks*

YOUNG, K. **Pneumonia in Adults. A Review of 203 Consecutive Cases.** *East African Med. J.* 1959, Mar., v. 36, No. 3, 133–46, 4 figs. [20 refs.]

The author discusses a large series of patients with pneumonia admitted to hospital in Hargeisa, Somaliland, in whom the clinical diagnosis of pneumonia was supported by radiological examination. His patients ranged in age from 15 to over 60 years [no information as to sex distribution is given]. This analysis was prompted by a previous clinical impression that in Zanzibar and Somaliland pneumonia in adults is a more benign disease than in Europe: this report appears to substantiate the earlier impression.

The distribution and extent of the inflammatory lesion in each patient is discussed. Lobar consolidation was confirmed in 89 out of the 203 patients; in 14 of these more than one lobe was affected. Compared with published experience elsewhere, in Somaliland involvement of the upper and middle lobes is more frequent, while the right lung is affected about twice as often as the left. Segmental consolidation was noted in 42% of patients, which is in proportion with English experience, but in 4 instances progression from segmental to lobar consolidation was observed. Lobular consolidation, indicated by diffuse mottling on X-ray, was discovered in both lungs in 19 patients and in only 1 lung in 10.

The leucocyte count was not as constantly raised as in European pneumonia, only 14·9% of patients showing a leucocytosis in excess of 15,000 per cmm. while in 8·4% a definite leucopenia was found. This was associated with a high incidence of complications.

Sputum culture was carried out in 159 instances, among which recognised lung pathogens were isolated in 74. The pneumococcus predominated (28 isolations), the staphylococcus was the next most frequent (19 isolated) and *Klebsiella pneumoniae* (14 isolations) was also common. *Mycobacterium tuberculosis, Escherichia coli, Proteus, haemolytic streptococci* and *Str. viridans* were each isolated in a few instances and were judged in each patient to have been the primary aetiological agent. *Klebsiella pneumoniae* was found in 6 patients whose lobar pneumonia was particularly severe and resistant to penicillin, and in 2 additional fairly severe examples of the disease whose response to penicillin was incomplete. In these patients a change of antibiotic to streptomycin caused rapid improvement, though cavitation occurred in 2 patients. Milder examples of *K. pneumoniae* pneumonia responded satisfactorily to sulphadimidine.

Complications comprised delayed resolution of unknown cause (14 examples), empyema (1), pleural effusion (2), pericardial effusion (2), staphylococcal cavitation (1), *K. pneumoniae* cavitation (1), persistent collapse (2), and meningism (1). [This seems a remarkably low incidence.]

In this series of 203 consecutive cases there were only 2 deaths [which bears out the author's contention as to the benignity of pneumonia in Somaliland]. Treatment was by penicillin or sulphadimidine, of which the former seemed slightly more effective. The author suggests that the mildness of the disease and the low mortality reflect the high resistance of the tough Somali

nomad, for only the fittest survive to adult life. A diet rich in animal protein and freedom from parasitic disease are equally important factors.

[For a previous study by the author, see this *Bulletin*, 1957, v. 32, 1140.] *J. H. Walters*

AUSTONI, M. La pneumopatie stafilococciche dell' adulto. [**Staphylococcal Pneumonia in Adults**] *Giorn. di Malattie Infettive e Parassit.* 1959, Jan., v. 11, No. 1, 13–33, 15 figs. [Numerous refs.]

This is a long and detailed account of the condition from the clinical point of view with illustrative cases and some good skiagrams of staphylococcal disease of the lungs. Some of the author's comments are of interest as examples of current Italian thought.

Resistance to antibiotics is regarded as of such importance that it must now be considered a definite biological characteristic. Staphylococcal osteomyelitis is now reasonably rare, but acute and chronic urinary, skin and lung conditions are common. The change in certain cases in the usual clinical manifestations can be explained by the fact that being caused by resistant organisms, they are likely to evolve in an unusual manner.

As regards staphylococcal respiratory disease, pneumonia due to this organism often follows virus A influenza. For diagnosis, together with the usual procedures an antibiogram is essential; in prognosis, much depends on age, the disease being worse in the very young and in the old, and on the source and type of the organism and whether resistant or not and if so to what extent.

In treatment, in spite of possible resistance antibiotics must be used, the first line being penicillin in large doses (1 mega every 3 hours) and chemotherapy should be associated with it especially sulphathiazole or its methyl derivatives. The route and manner of administration of drug or antibiotic are of capital importance, including intravenous, or intrabronchial (either direct or by aerosol), or administration by slow intravenous infusion of large doses. Chloramphenicol can be very useful (0·25 gm. every 4 to 6 hours). There may be some synergic action between it and gamma globulin. Cortisone or other steroids must be used with very great care, but in small doses for a short time they may be of help. If there is no response within 72 hours at the latest the antibiotic must be changed, *e.g.* to novobiocin, spiramycin, oleandomycin, etc. 2 antibiotics together are often better than one to overcome resistance. Surgery may be useful.

Austoni concludes that staphylococcal pneumonia in adults is of great importance as its incidence is continually increasing. *W. K. Dunscombe*

GOLDSTEIN, G. S. & WEHRLE, P. F. **The Influence of Socioeconomic Factors on the Distribution of Hepatitis in Syracuse N.Y.** *Amer. J. Pub. Health.* 1959, Apr., v. 49, No. 4, 473–80. [18 refs.]

The data in this study comprised 116 cases from Syracuse City Hospital and 463 cases from the Syracuse City Health Department which were recorded during the 5 years 1953–7. Only 1·9% of the City Hospital patients had a history of administration of blood or blood products within 6 months of admission and it appears that the disease was hepatitis A. The ages of the patients ranged from 6 weeks to 80 years. The highest attack rate, 6·2 per 1,000, was at ages 5–14 and these ages included 37·5% of all cases. The attack rate showed a secondary rise at ages 30–39, the group that included the parents of the children attacked. The case fatality was low, 1·6% for all ages, and no deaths were recorded under age 30. At ages 50–59 and 60 + the percentage fatality was 13·0 and 22·2 but there is in this age-group a liability to error in diagnosis, particularly confusion with malignancy. An analysis of the data by socio-economic indices showed that children in the lower social classes had a higher attack rate than children in the other groups while the adults had a lower rate despite the heavier family and community exposure. An attempt was made to establish the source of infection. No contact was traced in about 1/5 of the cases and family, neighbourhood or community type of contact was found in the remainder. Schools do not appear to have been of any importance in the spread of the infection. The lower social groups had the greatest amount of neighbourhood and family contact while the more diffuse community contact was more prevalent in the other classes.

The authors suggest that infection is influenced by crowding, poorer hygiene and sanitation and this may account for the greater infection of children and the higher immunity of adults in these circumstances.

W. J. Martin

BJERKEDAL, T. Epidemisk hepatitt. Smitteforhold under en epidemi i et landdistrikt. [**Infectious Hepatitis. Mode of Transmission in a Rural Area in Norway**] *Tidsskr. f.d. Norske Laegeforening.* 1959, May 1, v. 79, No. 9, 523–34, 6 figs. [38 refs.] English summary.

An outbreak of epidemic hepatitis having started in the latter part of 1955 in a rural community 40 miles from Oslo, Bjerkedal was sent to study it on the spot in January 1956. He visited 273 homes, taking stock of their 1,042 occupants with special reference to any previous attack of jaundice they may have had as well as to their present state of health. In this way he contacted 24% of the total population of the district. Among the 1,042 were 156 with a history of jaundice dating back with only one exception to the war years or earlier. In 114 homes involved in the present outbreak there were 510 occupants including 56 with a previous history of jaundice. Only 3 of the 56 developed hepatitis on this occasion. As Table 9 shows, there should in theory have been 17, not 3, such cases had not the earlier attack conferred some immunity.

Bjerkedal traces many of his cases to a 34-year-old mechanic whose access to the local water supply might account for several cases down stream. Here he sees a clue to the prevention of similar outbreaks in the future. He is less cheerful over the outlook for the prevention of contact cases which under ordinary conditions are the most numerous. Much can, however,

be done in his opinion if infected families would behave as potential sources of new infections and avoid public meeting places. *Claude Lillingston*

BALMUŞ, G., MITROIU, O., MARINESCU, G., VĂTĂŞESCU, A. & DUVAN, X. Cercetări asupra valorii reacţiei de aglutinare virus-bacterii (A.V.B.) în diagnosticul precoce al hepatitelor epidemice. [**Investigations of the Value of the Agglutination of Virus-Coated Bacteria (A.V.B.) Test in the Early Diagnosis of Infective Hepatitis**] *Studii si Cercetări Inframicrobiol., Microbiol. si Parazitol.* 1957, v. 8, No. 4, 539–49. [21 refs.] French summary.

An agglutination test with virus-coated bacteria has been widely used in the Soviet Union for the diagnosis of infective hepatitis. A heat-killed suspension of *Salmonella typhi* is incubated for 20 hours at 6°C. with acute-phase serum from a patient suffering from infective hepatitis; the virus, which is presumed to be adsorbed to the bacteria, is then detected in conventional agglutination tests with convalescent-phase serum. The authors have investigated the value of the tests in a modification in which haemolysed blood is used as the presumed source of virus and *Chromobacterium prodigiosum* is used as the supporting organism. Positive results were obtained in 44·8% of 184 and 19·2% of 52 tests of acute-phase blood with immune sera prepared by inoculating rabbits intravenously with blood taken from patients with infective hepatitis between the 3rd and 8th days of jaundice, and also in 13·7% of 51 tests against 3 convalescent-phase human sera; negative or doubtful results were obtained with organisms treated with 28 sera from patients with other diseases of the liver and in 32 tests with normal sera. *D. J. Bauer*

HAVENS, W. P., Jr. **Hemagglutination in Viral Hepatitis.** *New England J. of Med.* 1958. Dec. 18, v. 259, No. 25, 1202–6. [11 refs.]

Sera obtained during the first 17 days of illness from 105 patients suffering from virus hepatitis were precipitated with 20 volumes of chilled acetone; the precipitate was recovered by centrifugation in the cold, extracted once with 20 volumes of acetone and twice with 20 volumes of ether, dried in the vacuum from a water pump and reconstituted in saline. The final products were diluted 1 : 40 with borate saline of *p*H 9·0, and examined in serial dilutions in the same fluid in haemagglutination tests with a 0·25% suspension of the red cells of 1-day-old chicks made up in a phosphate buffer solution of such a composition as to give a final *p*H of 6·0 when added to the serum dilutions. 54 sera had been stored at dry ice temperature for 1–12 months before treatment, and 47 caused haemagglutination in titres of 40–1280; the remaining 51 sera had been stored for 6–8 years, and 22 gave haemagglutination in titres of 40–160. Titres up to 2,560 were obtained with 10 of 49 sera from patients with chronic liver disease, up to 320 with 20 of 58 sera from patients with other diseases, and up to 80 with 9 of 56 sera from normal persons. No haemagglutination was obtained with 23 sera from patients with obstructive jaundice. The haemagglutinin of the treated sera withstood heating at 56°C. for 6 hours with little loss of titre, and in starch electrophoresis experiment was found to migrate with the gamma globulin. *D. J. Bauer*

CAJAL, N., BOERU, V., BABA, C., LEONESCU, M., TUDOR, V. & LITMAN, S. Date obţinute cu ajutorul reacţiei aldolazei în hepatita epidemică. [**Results Obtained with the Aldolase Reaction in Infective Hepatitis**] *Studii si Cercetări Inframicrobiol., Microbiol. si Parazitol.* 1958, v. 9, No. 1, 9–14, 3 graphs. [10 refs.] French summary.

An investigation has been made of the aldolase activity of 300 samples of sera obtained from 115 patients suffering from infective hepatitis, 48 with other diseases and 44 normal persons. Mean values of 61·60 units were obtained in infective hepatitis, 24·16 in chronic hepatitis, 23·6 in obstructive jaundice, 19·25 in haemolytic jaundice, 21·8 in other acute virus infections, 12·57 in other conditions and 13·22 in normal persons. In 36 patients with infective hepatitis the serum aldolase activity was determined at intervals during the course of illness; a mean value of 90·20 units was observed during the 1st week, which declined steadily to attain 33 units after the 3rd week. In determinations carried out after the 3rd week of illness higher values were observed in patients with severe (87·7 units) and protracted (81·7 units) forms of the disease than in patients with infective hepatitis of moderate severity (37 units). *D. J. Bauer*

VERHEIJ, P. & VERLOOP, M. C. Acute trombopenische purpura bij mononucleosis infectiosa. [**Acute Thrombopenic Purpura as a Complication of Infectious Mononucleosis**] *Nederl. Tijdschr. v. Geneesk.* 1959, May 23, v. 103, No. 21, 1115–17, 1 fig. [10 refs.]

The English summary appended to this paper is as follows:—

"In a case of infectious mononucleosis complicated by acute thrombopenic purpura, severe menorrhagia occurred, which lasted for 17 days. Treatment consisting of blood transfusions and prednisone was successful."

CREDITOR, M. C. & MCCURDY, H. W. **Severe Infectious Mononucleosis treated with Prednisolone.** *Ann. Intern. Med.* 1959, Jan., v. 50, No. 1, 218–22, 1 fig.

A patient with severe infectious mononucleosis, with extreme pharyngeal lymphoid swelling such as to make respiratory obstruction imminent, was treated with an intravenous infusion of 50 mgm. prednisolone in 2 litres of dextrose solution, followed in the next 4 days by diminishing doses of prednisolone by mouth, antibiotic coverage also being given. The response was dramatic; within 12 hours the pharyngeal obstruction was improved, the temperature fell and the patient became alert and cheerful. By the 4th day of treatment the tonsils had returned to normal size, and the patient was well and was discharged on the 10th day.

This type of reaction to steroid treatment has previously been reported [this *Bulletin*, 1953, v. 28, 783; 1956, v. 31, 9], and may be life-saving in severe anginoid cases of this kind. *H. Stanley Banks*

MUNRO, D. D. **Eczema Herpeticum (Kaposi's Varicelliform Eruption) in an Adult.** *Lancet.* 1959, Apr. 11, 763–4.

A male student, aged 18, with a history of Besnier's prurigo since infancy with recurrent attacks of eczema and asthma, developed a red non-vasicular rash of his upper lip. He continued his holiday activities which included swimming and sunbathing and 2 days later a severe weeping eruption broke out over his head and face. A day later a crop of varioloid lesions developed on his nose and on his neck and upper chest. From these *Staphylococcus aureus*, haemolytic streptococci and herpes simplex virus were grown. His treatment included local hydrocortisone lotions and 1·5 gm. gamma globulin intramuscularly. *A. B. Christie*

LEIBOLD, J. E. **Herpes Simplex Keratitis following Febrile Illnesses.** *U.S. Armed Forces Med. J.* 1959, May, v. 10, No. 5, 570–73.

A discussion and account of 5 cases.

MARTIN, W. J. **Statistical Aspects of Poliomyelitis in England and Wales in Recent Years.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1959, Apr., v. 18, 54–64.

In England and Wales in 1950–7 there were 35,121 notifications of acute poliomyelitis. In each of the 8 years the number of notifications of males exceeded that of females and this was also true when only paralytic cases were considered. Relatively, however, the proportion of paralytic cases in the total notifications for each year was greater for females than for males. For the whole period there were 19,596 male notifications (an attack rate of 115 per million of the population) of which 12,255 (62·5%) related to paralytic cases, and 15,525 female notifications (85 per million) of which 10,453 (67·3%) related to paralytic cases. In each year there were more deaths among males than among females, the ratio (male : female) rose steadily from 1·27 : 1 in 1950 to 1·87 : 1 in 1954 and then fell slightly (1·65 : 1, 1·48 :1 and 1·72 : 1 in the last 3 years). Over the whole period there were 1,321 male and 892 female deaths representing 10·8% of male and 8·5% of female paralytic cases.

Notification rates are tabulated for each sex and year for paralytic and non-paralytic cases separately in 5 age-groups, 0–4, 5–9, 10–14, 15–24 and 25 years and over. In each year the attack rates were higher in males than in females in each age-group except 15–24 for paralytic disease, 25 and over for non-paralytic disease and a few odd years in other age-groups—there was very little sex difference in the rates in these exceptional groups. The attack rates for paralytic disease were highest at ages 0–4 and decreased as age advanced whereas the maximum rates for non-paralytic notifications occurred at ages 5–9 after which they decreased.

The number of paralytic cases is expressed as a percentage of all notifications for each sex and year in 7 age-groups, under 1, 1–2, 3–4, 5–9, 10–14, 15–24 and 25 years and over. For males for all years combined these percentages were 81, 80, 63, 53, 48, 60 and 73 respectively, while for females they were 87, 83, 69, 61, 55, 62 and 70. There was, however, considerable variation between years, the main constant feature being the high proportion of paralytic cases at preschool ages.

Analysis of fatality ratios (deaths as a percentage of paralytic cases) revealed an increase in the average ratio for the whole period as age advanced in both sexes. Thus in males the fatality ratios were 5·1, 6·5, 7·7, 15·8 and 24·6% at ages 0–4, 5–9, 10–14, 15–24 and 25 years and over, while in females they were 4·1, 5·4, 7·0, 13·1 and 16·7% respectively. Over the 8 years the fall in the fatality ratio has been relatively much greater among the young than among the old. Thus among males at ages 0–4, the ratio fell from 8·9% in 1950 to 1·6% in 1957 compared with a fall from 29·6% in 1950 to 22·2% in 1957 at ages 25 and over. Among females the ratios fell between 1950 and 1957 from 6·5 to 1·3% at ages 0–4 and from 23·0 to 13·1% at ages 25 and over.

Notification rates for each year for paralytic and non-paralytic cases are also tabulated for the Registrar General's regions and density areas. Generally the southern regions experienced heavier attack rates than the northern regions. The author notes certain points of interest arising from this area analysis and examines some areas in detail. Attack rates in Wales were often relatively low and over most of the period those in the south west were relatively high. The experience of Bristol with 4 large outbreaks in the 8 years largely contributed to the high rates in the south west.

E. A. Cheeseman

IONESCO-MIHĂIEŞTI, C., SGÂNDĂR, P. & BIBERI-MOROIANU, S. Quelques considérations epidémiologiques sur l'évolution de la poliomyélite en Roumaine. [**Epidemiological Observations on the Course of Poliomyelitis in Rumania**] *Arch. Roumaines Path. Expér. et Microbiol.* 1957, June, v. 16, No. 2, 161–70, 4 figs.

In the year 1927–8 Rumania experienced its first large epidemic of poliomyelitis with over 2,200 cases and an attack rate of 11·3 per 100,000. For the next 21 years the disease was rarely reported and the rates were never more than 2·6 per 100,000. In 1949, when the rate was again over 10, a new phase developed with shorter intervals between epidemics, higher epidemic levels and in 1956 the largest epidemic yet reported with a rate of 18·7 per 100,000 for the whole country. The recent epidemics were unevenly distributed and new areas were affected in each year. In 1956, 5 scattered regions with only one-quarter of the total population contributed 60% of the cases, and some districts had rates of over 100 per 100,000. Rates were in general higher in towns than in villages, though 65% of the cases were in rural areas. In some isolated

agricultural communities explosive outbreaks occurred, in one of which all the 17 children in the area were infected within 18 days by an adult contact, the grandmother of a sick child.

The 1956 epidemic had a typical seasonal distribution; the incidence rose in June, reached a peak in September and October and declined slowly through the winter months. Previous epidemics had ended more abruptly. Most of the patients (68%) were children under 3 years of age, while only 6% were over 15. 96 cases in children under 6 months of age were reported. In general, the patients in rural areas were younger than those in urban areas. A spinal distribution of paralysis was seen in 64% of patients, mainly in young children, and cranial nerve involvement in 16%, mostly in adults. Respiratory involvement occurred in 8%, while 12% were non-paralytic. The fatality rate was 7·4%, and was highest in those over 15.

J. Knowelden

Ionesco-Mihăieşti, C., Sergiesco, Dina, Klein, R., Horodniceanu, F., Zamfiresco, M. & Buimovici, Elena. Recherches sur la poliomyélite en Roumanie en 1956. I. Distribution des types antigéniques du virus poliomyélitique. [**Studies on Poliomyelitis in Rumania in 1956. I. Distribution of Antigenic Types of Poliomyelitis Vaccine**] *Arch. Roumaines Path. Expér. et Microbiol.* 1957, June, v. 16, No. 2, 171–7. [26 refs.]

During the course of the 1956 epidemic of poliomyelitis in Rumania, 531 stool specimens from patients and from contacts were examined on HeLa cells and monkey kidney tissue culture, and 94 strains of poliovirus were isolated. Poliovirus was also isolated from 20 of the 44 spinal cords of patients who died and in whom the diagnosis of poliomyelitis had been confirmed histologically. Of the total of 114 isolations, 110 were of Type 1, 1 of Type 2 and 3 of Type 3. The techniques used are discussed.

J. Knowelden

Ionesco-Mihăieşti, C., Horodniceanu, F., Sergiesco, Dina, Klein, R. & Marcovici, M. Recherches sur la poliomyélite en Roumanie, en 1956. II. Considérations épidémiologiques et détermination des types de virus dans un foyer limité de poliomyélite. [**Studies on Poliomyelitis in Rumania. II. Epidemiological Considerations and Determination of Virus Type in a Limited Outbreak**] *Arch. Roumaines Path. Expér. et Microbiol.* 1957, June, v. 16, No. 2, 179–83.

In May 1956 a localized outbreak of poliomyelitis started among children who had been in hospital in an area of Rumania where there had been few reported cases in earlier years. It was possible to trace the spread of infection from person to person among most of the sick children. Early in June 21 stool specimens were obtained from some of the patients and their contacts. Poliovirus Type I was isolated from 5 of the 10 specimens from patients and from 2 of the 11 specimens examined from contacts. Failure to isolate from some of the patients may have been due to the long interval, over 3 weeks, between the onset of illness and the taking of the specimen. 2 healthy contacts, from whom no poliovirus was isolated, were shown by guinea-pig inoculation to be excreting Coxsackie virus.

J. Knowelden

Blair, D. M. **Poliomyelitis: Southern Rhodesia, 1957.** *Central African J. of Med.* 1958, Feb., v. 4, No. 2, 49–60, 3 graphs.

In 1957 Southern Rhodesia experienced a severe epidemic with 663 reported cases, beginning early in the year about 2 months later than that in South Africa. The non-African population had 113 paralytic and 94 non-paralytic cases, with the corresponding attack rates of 54·6 and 45·4 per 100,000 at all ages. For the first time the number of cases in Africans, 443 paralytic and 13 non-paralytic, exceeded that in non-Africans, giving rates of 18·8 and 0·6 per 100,000. Although rates were lower in Africans than in non-Africans, the difference was far less than in previous years. Among non-Africans one-third of the patients were under 5 years of age, one-third 5–14 years and one-third 15 years and over; by contrast the African patients were younger with 86% under 5 years and only 5% 15 and over. Among non-Africans and Africans living in urban areas the epidemic reached a peak in March and April and then declined steeply. Among Africans in rural areas it developed more slowly and after an April–May peak declined slowly through the rest of the year.

Poliomyelitis vaccination of the non-African population 1–15 years of age was carried out on a large scale from March 1957 and was offered to African children 1–5 years of age in May. Arrangements for distribution varied, and although much was subsidized, in only a small proportion was it completely free of charge. In total about 170 litres were distributed to non-Africans and 30 litres to Africans, and whereas most of the 65,000 non-African children probably received 2 doses, many African children did not return for their second dose. The absence of uniform administrative arrangements and records provided no opportunity for an assessment of the protective effect of vaccine, or a surveillance of untoward reactions.

J. Knowelden

Hall, W. J., Nathanson, N. & Langmuir, A. D. **The Age Distribution of Poliomyelitis in the United States in 1955.** *Amer. J. Hyg.* 1957, Sept., v. 66, No. 2, 214–34, 10 figs. [40 refs.]

After the announcement in April 1955 of the successful results of the 1954 Poliomyelitis Vaccine Field Trials [this *Bulletin*, 1955, v. 30, 663, 951], vaccination programmes were undertaken in school clinics throughout the United States. By mid-June about one-half the 6–9-year-old children had received at least one dose, and of these about one-third had been given second doses. Failing adequately controlled studies for comparing poliomyelitis attack rates in vaccinated and unvaccinated children, the Communicable Disease Center of the Public Health Service, as an alternative method of assessing effectiveness, invited state health departments to take part in an Age Distribution Analysis of cases reported in their areas. 34 states and 3 territories

cooperated and their data are compared with information on cases in the 1952 epidemic available from 22 states.

In each of the 2 years the paralytic attack rates calculated for single years of age rose rapidly to a maximum at ages 2–5. The 1952 curve declined gradually after age 6 and levelled off at ages 10–14. In contrast the 1955 curve showed a marked trough at ages 7 and 8, but followed the 1952 pattern in older children. As vaccination was concentrated mainly in first and second grade schoolchildren, who would have been 7 and 8 years old in late summer at the height of the 1955 epidemic, this trough is believed to constitute evidence of vaccine effectiveness against paralytic poliomyelitis. It was estimated that at these ages attack rates in 1955 were about 33% below expectation based on the 1952 data, and as only about one-half this group were vaccinated this would correspond to vaccine being about 66% effective. This estimate should in any case be lower than the figure of 72% protection obtained in the Field Trials as many of the children vaccinated in 1955 received 1 injection only.

The age patterns of attack rates for non-paralytic illnesses were similar in 1952 and 1955 and showed no trough at 7 and 8 years of age in the later year. This might be partly because vaccine did not influence this type of illness or because the so-called non-paralytic group was heterogeneous and included cases of non-bacterial meningitis due to other agents.

J. Knowelden

PAUL, J. R. **Endemic and Epidemic Trends of Poliomyelitis in Central and South America.** *Bull. World Health Organization.* Geneva. 1958, v. 19, No. 4, 747–58, 4 figs. [16 refs.]

PAYNE has previously shown an inverse relationship between infant mortality rates and poliomyelitis morbidity [Third International Conference on Poliomyelitis, see this *Bulletin*, 1956, v. 31, 1196]. This study using data for 3 periods, 1940–4, 1945–9, and 1950–4, from 22 countries in Central and South America, confirms this general association, that where the infant mortality is above 75 per 1,000 live births the incidence of poliomyelitis is usually below 2 per 100,000. One group of exceptions, countries with high infant mortality and high poliomyelitis morbidity, such as Chile and Costa Rica, is difficult to explain. The other exceptions, countries with low infant mortality and low poliomyelitis morbidity, might fall into this category because of poor reporting of infectious disease. In 2 instances, however, epidemics of poliomyelitis developed subsequently so that they then conformed to the general pattern.

J. Knowelden

ENGELHARD, W. E. & BANCROFT, P. M. **Serological Studies of the Poliomyelitis Epidemic in Huskerville, Neb.** *J. Dis. Children.* Chicago. 1959, Apr., v. 97, No. 4, 409–17.

Previously the authors described an outbreak of poliomyelitis in Huskerville, Nebraska, probably due to faecal pollution of the water supply [this *Bulletin*, 1958, v. 33, 1020]. They now report serological studies on people living in the severely hit parts of the town, in the less severely hit and on a control group of children 6 months to 13 years of age who moved into the town 12–18 months after the epidemic. The studies showed that Type 1 virus was mainly responsible for the outbreak, that the virus was more widely distributed than clinical cases, but that the incidence of infection was highest in the areas which bore the brunt of the clinical cases. The control children showed a much lower incidence of poliovirus antibodies particularly to Type 1 virus and in the children aged 1–4 years. Although Type 1 virus was the main infecting agent the incidence of Types 2 and 3 antibodies was also higher in the children who experienced the epidemic and for Type 2 the incidence was higher in children living in the areas more seriously affected judged by clinical cases.

A. J. Beale

SOARES, M. A epidemia de poliomielite de Buenos Aires. [**Epidemic of Poliomyelitis in Buenos Aires**] *Rev. Assoc. Méd. Minas Gerais.* 1957, Mar. & June, v. 8, Nos. 1/2, 57–66. 1 plan & 6 figs.

This is a general description of the organization of hospital and public health facilities to deal with an epidemic of poliomyelitis in Buenos Aires in 1955–6. No epidemiological details are given and clinical details are brief. The administrative structure is given in a plan. Advice to contacts follows the usual lines concerning personal hygiene and avoidance of exercise. Respiratory cases were dealt with by well recognized methods—iron lungs, cuirasses and rocking beds were available: postural drainage and tracheotomy were practised where indicated. The equipment required for dealing with 20 patients is tabulated and is on a fairly lavish scale—20 iron lungs, 6 cuirasses, 6 rocking beds, 2 spirometers, 1 aspirator for every 2 patients, and 6 apparatuses for preparing compresses.

A. B. Christie

SIEGEL, M., GREENBERG, M. & BODIAN, J. **Presence of Children in the Household as a Factor in the Incidence of Paralytic Poliomyelitis in Adults.** *New England J. of Med.* 1957, Nov. 14, v. 257, No. 20, 958–65, 4 figs. [38 refs.]

This study is based on the 933 patients 15–44 years of age reported with paralytic poliomyelitis in New York City in the years 1949 to 1953. Average annual incidence rates were higher for males at 15–19 years, as it is generally in childhood. At 20 and over the male preponderance disappeared and in the 25–29-year age-group the rate was significantly greater in women than in men. From age 20 onwards the incidence was about twice as great in married as in single women; comparable data for men by marital status were not available. Although pregnant women were found to have higher rates than non-pregnant women, this did not account for the excess as non-pregnant married women had nearly twice the rate of single women.

A further analysis showed that for both sexes paralytic poliomyelitis was commoner in households with children under 15 years than in those without. The

excess in households with children was of about one-third for men and for non-pregnant women, but for pregnant women was much greater so that the rates were 2 to 3 times as great. Omitting those under 20 years, in which the number of married and pregnant women was small, and those over 39 years, in which the incidence of paralytic poliomyelitis was very low, the following table for persons of 20–39 years summarizes, by age-standardized rates, the relative risks in the different groups of the population:—

Group	Rate per 100,000		
	No children	1 child	2 or more children
All males	3·4	3·9	4·7
All females	3·3	5·1	5·5
Single females	2·6	2·9	3·5
Married females, non-pregnant	4·4	5·1	6·1
Married females, pregnant ...	3·4	11·2	7·5

J. Knowelden

PAFFENBARGER, R. S., Jr., with the assistance of V. O. WILSON, J. I. ENGLER, R. L. J. KENNEDY & O. W. MCBRIDE. **The Effect of Prior Tonsillectomy on Incidence and Clinical Type of Acute Poliomyelitis.** *Amer. J. Hyg.* 1957, Sept., v. 66, No. 2, 131–50. [38 refs.]

The tonsillectomy status of patients reported to have had poliomyelitis in Olmsted County, Minnesota, in 1952, and of their familial and extrafamilial contacts was obtained by postal questionnaires sent out in 1954 and 1955. At ages 0–4 tonsillectomy was infrequent in both patients and contacts, but in each subsequent age-group tonsillectomy was commoner in the poliomyelitis patients than in their familial or extra-familial contacts. The age-specific proportions among contacts were furthermore very similar to those in a sample of adult residents randomly selected from a directory. Dividing the patients into 4 occupational groups showed a gradient from highest tonsillectomy rates in the skilled to lowest in the unskilled groups, but in each group the rate for patients exceeded that for the corresponding contacts or survey population. The proportion tonsillectomized was just over 60% for patients with bulbar and bulbospinal poliomyelitis compared with about one-half that proportion in patients with spinal and non-paralytic types, and in the contacts who had no illness. The distribution of intervals since tonsillectomy was, however, similar in all these groups with very few performed less than 1 year before onset, and the indications for the operation were also alike. It was estimated that in the County the attack rate for bulbar and bulbospinal poliomyelitis was over 6 times as great in tonsillectomized as in non-tonsillectomized individuals, while for other forms the attack rate was unaffected by tonsillectomy.

The 1952 epidemic in Olmsted County was due to Type 1 poliovirus, but a study of an epidemic in Washington, D.C., in 1954 due to all 3 types, produced very similar results. In addition it was shown that nearly all tonsillectomized bulbar and bulbospinal cases had initial involvement of the 9th or 10th cranial nerve. On the other hand, a study of patients suffering from St. Louis encephalitis in Hidalgo County, Texas, in 1956 revealed no excess of tonsillectomy compared with household contacts and near neighbours of the same age.

It is concluded that these studies confirm the specific relationship between tonsillectomy and increased incidence of bulbar form of poliomyelitis some years later [this *Bulletin*, 1955, v. 30, 13, 844]. *J. Knowelden*

SALK, J. E. **Preconceptions about Vaccination against Paralytic Poliomyelitis.** *Ann. Intern. Med.* 1959, Apr., v. 50, No. 4, 843–61, 24 figs. [12 refs.]

In this James D. Bruce memorial lecture delivered before the American College of Physicians in April 1958 Salk reviews the present status of killed polio-vaccine. He recalls that many people thought (and some still do) that the only effective method of controlling poliomyelitis would be by means of a living attenuated vaccine. The achievements of the killed vaccine are confidently set out in a series of figures. It is shown that the primary response depends upon the potency and number of doses of vaccine; that 7 or more months after the primary course a booster type response occurs. This response and the duration of the maintenance of antibodies depends upon the adequacy of the primary course. A survey of the results of the effect of vaccine on the level of antibodies in the population was carried out in Pittsburg in 1956. Before vaccination 18% lacked antibodies to all 3 types (less than 1/64), after 2 doses 7·4% and none after 3 doses. After 3 doses 98·5% had antibodies (over 1/64) to all 3 types. [Results for children tested in the spring of 1958 are less impressive. See Salk, this *Bulletin*, 1959, v. 34, 734.] Data on 2 children are presented to show that antibodies persist for 3 or 4 years after a 3-dose course of vaccine. It is thought that the secondary accelerated response may be an important factor in preventing paralysis in immunized individuals. The decline in poliomyelitis in the U.S.A. is illustrated. It is thought possible that there may be a greater effect due to vaccine than can be accounted for by the number of people immunized. This could be due to the prevention of transmission of virus by vaccinated individuals. It is noted that faecal excretion of virus is not influenced by killed vaccine [although hyper-immunization of chimpanzees by vaccine does diminish faecal carriage, HOWE *et al.*, *ibid.*, 1958, v. 33, 824] but it is suggested that pharyngeal transmission may be very important in the spread of virus in hygienic communities and that as described by WEHRLE *et al.* [*loc. cit.*] pharyngeal excretion of poliovirus is limited by killed vaccine.

[It may well be true that an adequate course of killed vaccine will impede the transmission of poliovirus in the community, but this has not yet been clearly established.] *A. J. Beale*

LIEBE, S. & WÖCKEL, W. Landrysche Paralyse nach Poliomyelitisschutzimpfung. [**Landry's Paralysis after Poliomyelitis Vaccination**] *Deut. med. Woch.* 1959, May 8, v. 84, No. 19, 909–12, 932. [19 refs.]

Reactions to vaccination against poliomyelitis are considered to occur much less frequently than with

other prophylactic injections. In a report from the United States published in 1957 it was stated that after over 70 million inoculations, apart from infrequent local reactions and some general disturbance, the only serious results were 2 cases of encephalitis, 5 of myelitis and 1 unexplained sudden death (*Pub. Health Rep.*, 1957, v. 72, 381). A fatal case of Landry's paralysis in a 4½-year-old girl in Zürich who was taken ill 2 days after the second inoculation has also been reported [this *Bulletin*, 1957, v. 32, 933]. In about 5,000 inoculations carried out by the authors of the present paper no important reactions had been observed until there occurred the case reported here. The patient was a girl nearly 3 years old who was given the first intracutaneous vaccination with Salk vaccine prepared in Switzerland. On the twenty-third day after the injection the child appeared to be tired and was noticed to stumble frequently as she walked. There is a detailed clinical account of the progress of an ascending paralysis which caused death about 10 days after the first signs of illness had been observed. The differential diagnosis between this case of polyradiculitis and poliomyelitis is described. At autopsy the diagnosis of polyradiculitis was confirmed. There is a considerable discussion of this case of Landry's paralysis following poliomyelitis vaccination.

M. E. Delafield

LOSSING, E. H. **Vaccination and the Decline in Paralytic Poliomyelitis.** *Canadian J. Pub. Health.* 1957, Nov., v. 48, No. 11, 449–53, 5 figs.

In 1950 only 284 cases of paralytic poliomyelitis were reported in Canada, but in subsequent years the total rose to a peak of 3,691 cases in 1953 and then declined progressively to 368 in 1956. This decline started before the poliomyelitis vaccination programme and cannot wholly be attributed to it. Between April, 1955 and early summer, 1956 about 1,800,000 children had been vaccinated, 90% with 2 or more doses. Most of the injections were given to primary schoolchildren. Whereas in the years 1952 to 1954 the peak paralytic attack rate was at 5–9 years of age, in 1955 and 1956 the peak was in the pre-school age-group. This change in age distribution is regarded as evidence of the effectiveness of the campaign.

[This argument is similar to that of LANGMUIR and his colleagues (this *Bulletin*, 1956, v. 31, 612) based on the 1955 experience in the United States. It loses some of its force because the relatively high attack rates in pre-school children in their latter years might have resulted largely because they were too young to acquire natural immunity in 1953.] *J. Knowelden*

MCLAREN, Anne. **The Effect of Vaccines and other Substances upon the Course of Neurotropic Virus Infection.** *J. Hygiene.* 1957, Dec., v. 55, No. 4, 527–43, 2 figs. [44 refs.]

These experiments were an attempt to study in the laboratory the possible mechanisms of provocation poliomyelitis, by using the viruses of encephalomyocarditis (EMC) and the GD VII strain of encephalomyelitis in mice and a mixture of pertussis vaccine with diphtheria APT. In mice injected intracerebrally with GD VII virus subsequent intramuscular injection of this mixed diphtheria-pertussis prophylactic had no influence on the course of the infection, but subsequent intracerebral inoculation of this prophylactic shortened the incubation period.

Intramuscular injection of GD VII virus into the hind limb of mice gives rise to flaccid paralysis strongly localized in the injected limb. This localization was unaffected by the injection of the prophylactic into the opposite limb, presumably because the paralysis resulted from the injected virus reaching the CNS by way of the sciatic nerve. When the virus was inoculated intravenously, intramuscular injection of the prophylactic did cause localization of paralysis. The localization of paralysis in mice inoculated with EMC virus did not seem to be influenced by the prophylactic given intramuscularly, but was by injection of normal mouse brain suspension.

In mice inoculated intramuscularly with GD VII virus injection of the prophylactic into the same limb increased mortality, particularly if given 24–48 hours after the virus. This effect was replaced by the opposite, some degree of protection, when the vaccine was a few months old. Intracerebral inoculation of the prophylactic also increased mortality after intramuscular GD VII virus.

The author discusses possible mechanisms in a neurotropic infection—

(1) that the paralysis is determined by the route of entry of virus, as in intramuscular GD VII virus inoculation;

(2) that the blood-brain barrier is lowered by intracerebral inoculation, as in the experiments described;

(3) that intramuscular injections disturb neurovascular relations and facilitate passage of virus from the blood stream locally or at the corresponding level of the cord;

(4) that such injections allow the passage of virus from the blood stream to damaged nerve fibres in the muscle;

(5) that these injections modify the physiology of the corresponding anterior horn cells and favour proliferation of virus.

Only the last 3 mechanisms are directly relevant to provocation poliomyelitis in man. The experiments described do not help to distinguish which is most likely. *J. Knowelden*

See also p. 932, BEN-EFFRAIM & LONG, **The Sensitizing Power of Diphtheria Prophylactics in relation to Poliomyelitis.**

DUCA, M., DUCA, E., TOMESCU, E. & OANĂ, C. Cercetări asupra rolului mustei de casă în transmiterea infecției cu virus Coxsackie. [**Investigations of the Role of Houseflies in the Transmission of Coxsackie Virus Infection**] *Studii si Cercetări Inframicrobiol., Microbiol. si Parazitol.* 1958, v. 9, No. 1, 31–41. [20 refs.] French summary.

Coxsackie virus of type A10 was isolated from houseflies collected in September and October in 3 of 5 localities in Rumania in which cases of Coxsackie virus

infection had been occurring. The isolations were made at a time when the virus could no longer be detected in the stools of persons who had recovered from the disease or who had been exposed to infection. Virus was present in faeces and regurgitations of houseflies infected experimentally by feeding on the carcasses of infant mice infected with type A10 Coxsackie virus, and could be detected over a period of 16 days. The virus remained viable in the faeces of flies for 37 days at room temperature. Attempts to demonstrate transovarian transmission gave negative results, and virus ingested by the larvae did not survive the process of pupation. *D. J. Bauer*

SUSSMAN, M. L., STRAUSS, Lotte & HODES, H. L. **Fatal Coxsackie Group B Virus Infection in the Newborn. Report of a Case with Necropsy Findings and Brief Review of the Literature.** *J. Dis. Children.* Chicago. 1959, Apr., v. 97, No. 4, 483–92, 10 figs. [32 refs.]

Another fatal case of Coxsackie B virus infection in a newborn infant is described, and the literature reviewed comprehensively [see also this *Bulletin*, 1959, v. 34, 114]. Coxsackie B virus (type undetermined) was isolated from a stored stool specimen by inoculation into suckling mice. All the mice inoculated with 7th passage material died with typical Coxsackie B lesions. The patient died on the 8th day of life after 5 days of illness characterized by fever, and first lethargy then irritability. No cardiac lesions were found in life. A full account of the pathological features is given. These are similar to those previously described. There was severe myocarditis and focal necrotic lesions with surrounding inflammatory response in the liver, adrenals, islet cells of the pancreas, pituitary, bone marrow and striated muscles. *A. J. Beale*

FOLEY, J. F., CHIN, T. D. Y. & GRAVELLE, C. R. **Paralytic Disease due to Infection with ECHO Virus Type 9.** *New England J. of Med.* 1959, Apr. 30, v. 260, No. 18, 924–6, 1 fig.

"A case of meningitis due to ECHO virus Type 9 associated with residual muscle weakness is presented. There is no evidence that the illness was associated with infection with poliomyelitis virus or with St. Louis encephalitis, western equine encephalitis, eastern equine encephalitis or lymphocytic choriomeningitis."

HILDES, J. A., WILT, J. C. & STACKIW, W. **Neutralizing Viral Antibodies in Eastern Arctic Eskimos.** *Canadian J. Pub. Health.* 1959, Apr., v. 50, No. 4, 148–51, 1 fig.

During 1957, 240 blood samples were collected from various Eskimo communities, mainly on Baffin Island, and tested for neutralizing antibodies at a $\frac{1}{4}$ dilution against the following viruses, ECHO 6 and 9, poliovirus Types 1, 2 and 3, adenovirus 3 and herpes simplex. Antibodies to herpes simplex were present in 95% of the samples, to ECHO 6 in 56% and ECHO 9 in 37%. It is concluded that herpes simplex virus, ECHO 6 and ECHO 9 are endemic in these communities. The distribution of poliovirus antibodies was very uneven, some communities—usually the more southerly—had a high incidence to all 3 types, whereas other communities had no antibodies to one or other of the 3 types. There was a rising incidence with age to poliovirus Type 3 in 3 communities and in one community for Type 2. Antibodies to adenovirus type 3 were present in 62% of the total samples. A comparison was made with the incidence of adenovirus complement-fixing antibodies (as a measure of recent as opposed to past infection) on the same sera which had been done as part of study of the incidence of complement-fixing antibodies to respiratory viruses carried out by the authors previously [this *Bulletin*, 1958, v. 33, 929]. In some communities most of the adenovirus infection was associated with a recent Type 3 epidemic whereas in other communities there was evidence of past infection with Type 3 or a related adenovirus. *A. J. Beale*

YAMAGIWA, S. & SATOH, H. **Encephalitis Epidemica Japonica in Horses occurring in a Non-Epidemic Year.** *Acta Path. Japonica.* 1957, Nov., v. 7, Suppl., 613–35, 3 text figs. & 16 figs. on 3 pls. [18 refs.]

This is a clinical and pathological description of 18 sporadic cases of paralytic disease in horses in Japan between 1955 and 1957. The duration of the disease varied from a few hours to 3 weeks. Some of the horses had been vaccinated against Japanese encephalitis. Japanese encephalitis virus is said to have been established as the cause in 2, 1 by isolation of the virus and the other by complement-fixation tests [but no details are given and no valid evidence of Japanese encephalitis infection is produced for the others]. *C. E. Gordon Smith*

HUANG, C. H. Cercetări asupra factorilor care determina infecții inaparente cu virusul encefalitei japoneze B. [**Investigation of Factors Causing Inapparent Infections with Japanese B Encephalitis Virus**] *Studii si Cercetări Inframicrobiol., Microbiol. si Parazitol.* 1957, v. 8, No. 4, 471–91, 3 figs. [15 refs.] French summary.

In an investigation of the pathogenicity for mice of 13 strains of Japanese B encephalitis virus the titres on subcutaneous inoculation were much lower than those found on intracerebral inoculation. The lowest subcutaneous titre was with the well-adapted Nakayama strain, and a mean of $<1{\cdot}3$ log unit was obtained with virus material covering 5 serial passages. In mice infected subcutaneously the duration of viraemia was directly related to the subcutaneous pathogenicity of the strain, lasting for 6 days in the Pekin strain and other strains with subcutaneous titres of 4–8 log units and for only 2 days with the Nakayama strain. The Pekin strain was more resistant to thermal inactivation at 37°C. than the Nakayama strain. The effect of environmental temperature upon virus in the vector was also studied; adult *Culex pipiens* var. *pallens* infected by feeding and maintained at 18–22°C. contained less virus than a similar group of mosquitoes maintained at 26–31°C., corresponding to ambient temperatures

observed during the epidemic season in Pekin. The results thus obtained from studies of the virus suggest that inapparent infections in man may be due to infection with a small dose of a strain of virus with low subcutaneous pathogenicity. *D. J. Bauer*

TRAPIDO, H., RAJAGOPALAN, P. K., WORK, T. H. & VARMA, M. G. R. **Kyasanur Forest Disease. Part VIII. Isolation of Kyasanur Forest Disease Virus from Naturally Infected Ticks of the Genus *Haemaphysalis*.** *Indian J. Med. Res.* 1959, Mar., v. 47, No. 2, 133–8. [11 refs.]

The ticks studied were collected by dragging "flags" in the Kyasanur Forest during 3 days in May 1957. Most of the ixodid ticks taken were immature *Haemaphysalis* species. Ground-up pools of ticks were inoculated into 2-day-old mice and 2 strains of virus were isolated from large pools of immature *Haemaphysalis*. Re-isolation of 1 strain was achieved.

Subsequently, between July and October 1957, 12 strains of Kyasanur Forest virus were isolated from pools of *Haemaphysalis spinigera* and 1 each from *H. turturis* and *H. papuana*. No isolations could be made from substantial numbers of ticks from outside the epidemic area, nor from ticks of the genera *Rhipicephalus, Dermacentor, Amblyomma, Boophilus*, or *Ixodes*.

[For earlier studies, see this *Bulletin*, 1958, v. 33, 105, 444: 1959, v. 34, 203.] *C. E. Gordon Smith*

DEREVITSKAIA, V. V. & GLUSHKOVA, M. R. **Biphasic Meningo-Encephalitis in the Moscow Oblast.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, Nos. 1/2, 204–8. [Translated from Russian.]

Between 1948 and 1956 small numbers of cases occurred in 4 villages and a labour settlement within 6 km. of each other and in close contact with forest. *Ixodes ricinus* is common in the forest. Many goats are kept in these villages and they are grazed in the forest. The disease occurrs in a short season, mainly in May and June, and its incidence parallels the activity of *I. ricinus*.

Goats whose milk is responsible for human infections are usually under 1 year of age and they excrete virus for 7–10 days. Cows' milk to which goats' milk had been added to improve the fat content was the source of one outbreak. Ticks were not very numerous on cattle in the area—the maximum of 10–23 per animal was reached in May.

The symptoms in man included biphasic fever in 60%, toxaemia, evanescent neurological symptoms, and haemorrhagic manifestations in a few.

Tick control in pastures was attempted with hexachlorane but was unsuccessful. DDT applied to goats in the form of a powder or paste markedly reduced their tick-infestation and appeared to diminish the incidence of human disease. *C. E. Gordon Smith*

VAN BOGAERT, L. **Acute Encephalitis in Childhood.** *Brit. Med. J.* 1959, May 9, 1199–1204.

Although the term "acute encephalitis" clearly suggests a "morbid process, inflammatory in nature occurring within the brain", the author points out that in the early stages at least, cerebral dysfunction is mediated by impairment of circulation and by the accumulation of toxic metabolites consequent to this, rather than by inflammation due to local bacterial or viral infection. It is only when signs of focal cerebral damage or of meningeal irritation declare themselves that one can assume the actual invasion of the brain by the pathogen.

Repeated vomiting, photophobia and neck rigidity will now be present, while ophthalmoscopy will show slight venous engorgement. Although the cerebrospinal fluid may still be cytologically and chemically normal, it will flow under increased pressure. This is the stage of acute serous meningitis and it is strongly suggestive of a viral or of a leptospiral meningoencephalitis. In the absence of signs of visceral disease outside the central nervous system one considers the possibility first of poliovirus infection, secondly of invasion by any of a host of viruses almost all of which are primarily zoonotic. A history of contact with a potential animal reservoir may give a clue as to the identity of the pathogen, of which examples are the horse, as a source of equine encephalomyelitis virus, mice, which may carry that of lymphocytic choriomeningitis, dogs or pigs, which may pass virulent leptospires in their urine, and sheep which may harbour the virus of louping ill [now known to be identical with that of Russian spring-summer encephalitis] or *Rickettsia burneti*, causing Q fever.

Viral invaders of the central nervous system usually give rise to a biphasic type of illness in which an initial febrile illness, lacking specific characteristics, marks the systemic invasion, while at a later stage focal signs and symptoms indicate that the organism has settled down at its site of election in the nervous system. This stage is accompanied by allergic manifestations as specific antibody formation rises to meet the invader. The protein content of the cerebrospinal fluid increases but the cellular reaction lags behind, while various colloidal reactions indicate increasing amounts of abnormal globulin. When death occurs at this stage the autopsy findings are unimpressive, they comprise degeneration of the cells of many parenchymatous organs with evidence of interstitial oedema: the whole picture is one of increased capillary permeability.

Acute haemorrhagic encephalitis may develop as an extension of serous encephalitis resulting from capillary engorgement and stasis, and may be precipitated by phlebitis of cortical veins or of the great cerebral venous sinuses. The clinical picture presented is fairly constant: nausea, sweating, hyperpyrexia, convulsions, coma and death; circulatory collapse may occur at any time. When cortical thrombophlebitis has supervened, monoplegia, hemiplegia or bilateral hemiplegia will usually be displayed. Thrombophlebitis of the cerebral veins may follow any form of cranial or facial sepsis, or it may complicate the exanthemata, typhoid fever or pure marasmus. Otitic hydrocephalus is a well known example of the process.

In many instances therefore there arises the doubt as to whether the disease process is a true inflammatory degeneration of the brain cells—an encephalitis, or is

a nerve cell degeneration induced by vascular impairment—an encephalopathy. Even at autopsy the differentiation is often impossible.

A clearer picture of encephalitis is that due to herpetic infection in infancy. This occurs in 2 forms, as a fulminating inflammatory degeneration of the liver and brain in neonatal life or as a pure encephalitis accompanied by cutaneous or mucosal herpetic lesions in later infancy. These fatal conditions result in a widespread necrotic encephalitis, most marked in the temporo-hippocampal regions. A further rare and obscure type of necrotizing encephalitis may be seen in later childhood and is associated with the presence of characteristic inclusion bodies of type A.

Insidious but progressive neurological manifestations due to degeneration of the white matter of the conducting tracts may follow at varying intervals any of the exanthemata or even influenza and are classified as leucoencephalitis. Their prognosis is usually favourable. This condition merges into the recognized types of late encephalitis and it is possible even that a small proportion of such cases represent the onset of disseminated sclerosis.

Treatment of the child suffering from an encephalitic syndrome presents great difficulty. Coma, convulsions, hypothermia or hyperpyrexia all demand appropriate management, while the suspicion of cerebral thrombophlebitis, in the author's opinion, justifies anticoagulant therapy. Acute viral encephalitis as well as the late manifestations of post-infectious encephalitis provide an indication for treatment with steroids or corticotrophin.

[This important but discursive and philosophical article is difficult to abstract, and those especially interested are advised to read the original.]

J. H. Walters

MAVOR, H., GALLAGHER, F. W. & SCHUMACHER, G. A. **Cerebrospinal-Fluid Culture in Multiple Sclerosis.** *New England J. of Med.* 1959, Apr. 23, v. 260, No. 17, 860–63.

"Cultures of cerebrospinal fluid from 12 patients with multiple sclerosis and 14 patients with other disorders, of which 9 and 11, respectively, were considered satisfactory, remained negative for evidence of growth of spirochetes during periods of incubation of at least thirty days.

"The failure to obtain growth of spirochetes in cultures of cerebrospinal-fluid specimens from patients with multiple sclerosis is at striking variance with a previous report of positive cultures in 78 per cent of such cases."

PUBLIC HEALTH LAB. SERVICE. **Frequency of carriers of Salmonellae, Shigellae, and Pathogenic Coliform Organisms in Normal Children under 5 Years. An Interim Report of the Public Health Lab. Service.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1959, May, v. 18, 86–91.

This report analyses the results obtained in some 20 laboratories of the Public Health Lab. Service of investigations relating to the carrier condition in salmonella, shigella and pathogenic coli infections. The average carrier rate for all salmonella infections in children of 1–5 years was 2 per 1,000, based on 8,000–9,000 samples. The figures for dysentery carriers (all were *Shigella sonnei* in type) were 4 per 1,000. The carrier rate in respect of the pathogenic coli was very much higher and was between 15 and 20 per 1,000; there was considerable variation in this group according to the particular serotype and the rate was higher in the age group 0–1 year than in the older children. The seasonal rates for the salmonella and shigella carriers closely followed the incidence of their associated diseases.

The results in general are in agreement with the findings of other workers [see, for example, this *Bulletin*, 1951, v. 26, 25; 1957, v. 32, 415; 1958, v. 33, 67].

H. J. Bensted

SEDLÁK, J. Zur Problematik der Salmonellosen in der ČSR. [**The Problem of Salmonella Infections in Czechoslovakia**] *Ztschr. f.d.g. Hyg. u. ihre Grenzgebiete.* Berlin. 1959, Mar.–Apr., v. 5, No. 2, 91–102, 3 figs. [29 refs.]

The problem of salmonella infections in Czechoslovakia is similar to that existing in other countries. Salmonellosis is not notifiable in Czechoslovakia, hence its true incidence cannot be ascertained. A table gives the numbers of proved cases during the past few years. In 1956 there were 1,290 cases of typhoid, 241 of paratyphoid B and 2,511 of other salmonella infections. The data are analysed with reference also to other published work by trend in the past few years and in relation to the incidence of other infectious diseases. Tables set out the number of epidemics of salmonella infection from 1939 to 1951 and the cause of each. Particular consideration is given to the potential danger of eggs and a table gives the salmonella types which have been isolated from the eggs and droppings of a number of different kinds of poultry. A very detailed table gives particulars of the frequency with which the very numerous salmonella types have been isolated in Czechoslovakia and these findings are compared with those recorded in the neighbouring countries.

M. E. Delafield

MEITERT, T., ISTRATI, G., NEGRU, Florica & LEONDARIE, V. Recherches sur le rôle possible de l'eau de la Mer Noire et du lac de Tékirghiol dans la transmission de certaines infections entériques. [**Investigations on the Part played by Sea and Lagoon-Water (Black Sea, Lake of Tékirghiol) in the Transmission of Enteric Infections**] *Arch. Roumaines Path. Expér. et Microbiol.* 1958, Sept.–Dec., v. 17, Nos. 3/4, 513–22.

The work described in this paper was undertaken as an epidemiological study of the extent to which the waters of the Black Sea and of Lake Tékirghiol could be incriminated in the spread of *Salmonella* and *Shigella* infections.

In the first part of the work more than 350 samples of water were taken from 26 different points during July to August 1956 and examined bacteriologically by methods which are described, but in no instance were dysentery or *Salmonella* organisms isolated.

The second part of the investigation—a study of the survival time of a number of laboratory strains of these organisms in different waters—was carried out because the Black Sea and the Lake both receive waste waters from a large number of bathing establishments and other possible sources of bacterial pollution. Different defined strains of Flexner, typhoid and paratyphoid A and B organisms were inoculated in varying numbers into sterilized and non-sterilized Black Sea and Lake water and also into well-water and water of a piped supply.

The results of these survival time experiments are described with several tables of numerical data. It was found that the survival time varies with the strain of organism and is shorter with small inocula than with large. Exposure to sunlight rapidly destroys the organisms and the high salt content of Lake Tékirghiol also brings about this rapid destruction. Survival did not usually exceed 1–2 days in non-sterilized water, which is considered to be due to the presence of the antagonistic saprophytic flora. *M. E. Delafield*

FROMME, W. Zur Epidemiologie der Salmonelleninfektion. [**The Epidemiology of Salmonella Infection**] *Ergebn. Mikrobiol. Immunitätsf.* 1959, v. 32, 161–95. [Numerous refs.]

This long paper consists mainly of a review of modern knowledge of *Salmonella* infections based on references to over 200 published papers. Separate sections contain descriptions of studies on salmonellae found in: (1) ducks' and hens' eggs, (2) natural waters, (3) birds, (4) other animals, (5) animals slaughtered for food, (6) human infections and (7) imported animal food-stuffs. The measures that have been adopted or should be introduced for the control of *Salmonella* infections are also considered at length. The mass of detailed information which is carefully presented is well summarized in a long but clear series of conclusions. *M. E. Delafield*

CALLIS, L. M. Epidemiología de la fiebre tifoidea en Barcelona. [**Epidemiology of Typhoid Fever in Barcelona**] *Rev. Sanidad e Hig. Pública.* Madrid. 1958, Sept.–Oct., v. 32, Nos. 9/10, 381–425, 10 figs. (4 on folding pls.)

Typhoid fever is endemic in Barcelona every autumn and sometimes in July and November as well. In the past 40 years 7,160 cases, 4,162 female and 2,998 male, have come to notice. In addition there is an unknown number of undetected cases. The common age range is between 20 and 40 years. The proportion of patients vaccinated previously against typhoid fever has fallen from 13·4% in 1944 to 1·2% in 1956: the interval between vaccination and the onset of the disease was usually over 3 years but in a number of cases it was within a year. A substantial number of the patients were infected outside the city: it was 13·9% in 1955 and 7·2% in 1956.

A table gives year by year since 1943 the probable source of infection. In 1956 direct infection from a known case accounted for 3·4%; crude shell fish, 2·1%; crude salads, 17·1% and water-borne, 20·7%. The last is unusual and only once before, in 1947 with 2·3%, does this vehicle of infection appear.

Maps and a table show the distribution of the cases for 2–7-year periods among the districts of the city.

A sharp and widespread epidemic caused 2,267 deaths in 1914–15. It was revealed that leaking drains had caused contamination of the public water supply. Cesspits were closed, drains sealed and new water mains laid; contacts were vaccinated against the disease and food handlers supervised. Since then several small outbreaks have occurred: they are described in detail including the steps taken to bring them to an end. Some were due to the use of contaminated water from private wells which had to be sealed off.

The case-mortality has fallen sharply: it was 22·3% in 1924–36; rose to 56% during the civil war and fell to 17% in 1939–45 and to 1·24% in 1951–5.

There is a good description of the public water supply and the steps taken to ensure its safety. Anti-typhoid vaccination is available and, whenever required, can be made compulsory for certain groups of people but the annual number vaccinated is only 3,000 among a population of nearly 1·5 million.

The methods used to investigate an outbreak, discover the source of infection and deal with it are those routinely observed in Western countries except that in only one outbreak was it mentioned that phage-typing was done and for this the specimens had to be sent to Paris. *Allen Daley*

VAIZEY, J. M. **Typhoid at Mulago. Analysis of Cases 1949 and 1957.** *East African Med. J.* 1959, Feb., v. 36, No. 2, 65–71, 3 figs.

There were 188 established cases of typhoid in Mulago Hospital, Uganda, in 1957 and during 1949 there were 200, an analysis of which has been published [this *Bulletin*, 1952, v. 27, 1096]. In 1957 chloramphenicol was available for the treatment of the disease but was not obtainable in 1949. The present paper compares the experience of typhoid in these 2 years. In both years the same diagnostic criteria, which are stated, were followed. Tables and figures with description set out the monthly incidence in each of the years from 1952 to 1957, the comparative analysis of the data for 1949 and 1957 by age, number of deaths, duration of illness and by number of complications.

The main differences between the experience of 1949 and 1957 were that the case mortality was reduced from 24·5% to 7·5% and the duration of fever and of stay in hospital were reduced by about 50%.

There is some discussion of the clinical experiences and also reference to the finding of a strain of *Salmonella typhi* which has proved to be almost completely resistant to chloramphenicol. *M. E. Delafield*

KIREYEVA, K. I., KHLYSTOVA, Z. K., SHARAPOVA, T. A., POLTAVSKAIA, N. K., KOLESNIKOVA, Z. K., MARTEM'IANOVA, P. M., GATILOVA, A. S. & ZHERDEVA, T. A. **Observations on the Epidemiology of Dysentery in Vladivostok.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, No. 10, 1587–91. [Translated from Russian.]

" (1) The incidence of dysentery in Vladivostok rose from 1949 to 1955 then fell in 1956 by 24·1 per cent as against the preceding year.

" (2) As a result of improvement in diagnosis of intestinal infections over the years under consideration, the proportion of dysentery cases to the total number of cases of intestinal infections has changed; in 1949 it was 1 : 2·2, whereas in 1955–56 it was 1 : 1·2.

" (3) The intensification of measures against dysentery has succeeded in reducing the proportion of cases among small children (under 2 years) from 67·3 per cent in 1949 to 37·8 per cent in 1956.

" (4) The proportion of chronic dysentery cases to the total number of cases of this disease was 8·2 per cent in 1956; 69·1 per cent of the cases of chronic dysentery were among children under 2 years of age.

" (5) The highest numbers of cases of intestinal infections, including dysentery, were recorded in August, September and October.

" (6) The rising proportion of cases occurring in major foci (29·1 per cent in 1949, 41·5 per cent in 1955) gives grounds for considering that in combating dysentery attention should first be given to eliminating micro-foci.

" (7) Among organisms causing dysentery isolated in Vladivostok, *Sh. flexneri* predominated (73·8 per cent); *Sh. sonnei* occupied second place (25·6 per cent), and *Sh. flexneri* var. *newcastle* accounted for 5·1 per cent of the total.

" (8) The death rate for dysentery, which in 1949 rose as high as 13·7 per cent, has fallen year by year to only 0·5 per cent in 1956."

NIKODEMUSZ, I. & ORMAY, L. Résultats des examens bactériologiques au cours d'une épidémie de dysenterie due à l'eau de consommation. [**Results of Bacteriological Examinations during an Epidemic of Water-borne Dysentery**] *Arch. Inst. Pasteur de Tunis.* 1959, Mar., v. 36, No. 1, 43–51, 1 graph.

The outbreak of bacillary dysentery described in this paper occurred in 1954 in a country district of Hungary. The organism responsible was found to be *Shigella flexneri* 2a and the outbreak was considered to be due to a contaminated water supply; it was, relatively, of an explosive nature and of short duration although secondary cases occurred among other patients, and the attendants, in the hospital to which the original dysentery patients were admitted. *Sh. flexneri* 2a was isolated from all the patients and contacts with clinical signs of dysentery, but also from a number at risk who showed no clinical signs. The particular strain of *Sh. flexneri* 2a isolated exhibited some degree of resistance to sulphaguanidine—the sulphonamide employed.

The outstanding feature of this outbreak was the considerable number of patients who continued to excrete the infecting organism long after the clinical condition had subsided. It was noted that those in whom there were no overt signs of dysentery more often became long-term excreters than those who contracted a typical acute clinical dysentery. Direct examination of the intestinal mucosa of the lower bowel suggested that the persistent excretion of the infecting organism was associated with the development of a chronic dysenteric infective condition.

[The observations recorded in this paper are by no means unique; they are the common experience of many investigators, but from the great amount of evidence available it would appear, as far as *Sh. flexneri* and *Sh. sonnei* outbreaks are concerned, that the infecting organism is frequently excreted over very long periods, whether from frank cases of dysentery or inapparent infections, without obvious lesions in the gut.] *H. J. Bensted*

BLAGOVESHCHENSKII, V. A., KONIKOV, A. P., KLIUCHEVA, V. V., MARMALEVSKAIA, L. I., TARKHANOVA, I. A., GEKKER, V. D., KOVALEVA, N. I., IVANOVA, L. K. & KASHINTSEVA, N. C. **The Preparation of a combined Chemical Depôt Vaccine against Enteric Infections and Tetanus. I. Preparation, Chemical Properties and Adsorption of Antigens.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, No. 10, 1572–5. [Translated from Russian.]

" (1) The chemical properties of antigens isolated from cultures of organisms of the enteric group grown on synthetic media, using a phenol extraction technique, are similar to those of Boivin's antigens. The yield of phenol antigens is, however, twice as high as that obtained by the Boivin technique.

" (2) With the observation of controlled conditions the phenol antigens were practically completely adsorbed on to aluminium hydroxide.

" (3) Adsorbed polyvaccine prepared from enteric antigens and from highly purified tetanus toxoid could be kept for a number of months without observable desorption of the antigens."

GEKKER, V. D., IVANOVA, L. K., KOVALEVA, N. I., KASHINTSEVA, N. C., BLAGOVESHCHENSKII, V. A., KONIKOV, A. P., KLIUCHEVA, V. V., TARKHANOVA, I. A. & MARMALEVSKAIA, L. I. **The Preparation of a Combined Chemical Depôt Vaccine against Intestinal Infections and Tetanus. II. Immunological Properties of the Chemical Combined Vaccine.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, No. 10, 1576–80, 1 fig. [Translated from Russian.]

" (1) Complete antigens isolated from enteric organisms by means of phenol extraction did not differ in their toxicity and serological properties from those isolated by the Boivin method.

" (2) Phenol antigens adsorbed on aluminium hydroxide are non-toxic.

" (3) Unadsorbed and adsorbed phenol antigens displayed marked immunogenicity.

" (4) Repeated immunization with small doses of adsorbed phenol antigens produced high immunity.

" (5) Purified tetanus toxoid adsorbed on aluminium hydroxide produced a high degree of immunity in immunized animals."

MITEL'MAN, S. L. & STAROVEROVA, A. G. **A Study of Reactions produced by a Chemical Combined Vaccine against Enteric Infections and Tetanus (IEM Polyvaccine) in Selected Groups.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, No. 10, 1580–82. [Translated from Russian.]

"(1) From the sum total of local and general symptoms the reaction of inoculated persons to IEM polyvaccine may be regarded as having little traumatic effect.

"(2) The mild reactions due to IEM polyvaccine allow it to be used in large-scale epidemiological investigations."

KHEIFETS, L. B., KILESSO, V. A., KAPLAN, A. E., GURALEVICH, G. S., TIMEN, I. E., SKROZNIKOVA, A. V. & GUSEVA, I. I. **Investigation of a Polyvalent Vaccine in an Epidemiological Experiment.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, No. 10, 1582–7. [Translated from Russian.]

The epidemiological experiment described in this paper was made on an adult population (16–60 years of age) comprising some 45,000 individuals, of whom some 16,000 served as controls. 3 polyvalent vaccines were used but it is difficult to appreciate the exact difference between them since details of preparation are not given; they all appear to be typhoid-paratyphoid-dysentery vaccines. The results indicate that the incidence of enteric fever in the immunized population was 1·6 per 10,000 as compared with 6·7 per 10,000 in the control group, and the figures for dysentery were 24 and 55 per 10,000 respectively. The authors report a relatively high proportion of reactions after the injection of the vaccines used, and although satisfied with the protection afforded by the procedures described consider that the question of the reactions after the injection of the vaccines should be investigated.

H. J. Bensted

BLACK, J. **Renal Tubular Damage in Infantile Gastro-Enteritis.** *Arch. Dis. in Childhood.* 1959, Apr., v. 34, No. 174, 158–65, 3 figs. [28 refs.]

Detailed case histories are given of 2 infants, aged 18 months and 12 weeks, in whom acute gastro-enteritis was accompanied by signs of renal tubular damage. In both the only urine abnormality on admission was slight proteinuria but this was followed by definite signs of tubular damage. Hypokalaemia was present in both infants and may have been a factor in causing the tubular damage. Reference is made to another study of 653 infants suffering from gastro-enteritis; in 21 proteinuria of 40 mgm. % or more was present: there was some evidence that proteinuria and severe dehydration were related. Proteinuria in an infant recovering from severe shock or dehydration should lead to a detailed investigation of renal function: daily weighing and repeated estimation of blood chemistry may be required in addition in order to assess daily requirements of fluid and electrolytes.

A. B. Christie

TS'AO, Yü-P'u, OUYANG, Tsung-Jen, P'AN, Yen-Jo & CHOU, Hua-K'ang. **Treatment of Infantile Diarrhea with Neomycin.** *Chinese Med. J.* Peking. 1959, Apr., v. 78, No. 4, 361–5.

This is an account of the use of neomycin in the treatment of infant gastro-enteritis. In 115 of 202 patients under 18 months old, pathogenic types of *Escherichia coli* were isolated. Neomycin in doses of either 50 mgm. or 25 mgm. per kgm. bodyweight per day was effective in causing the disappearance of the symptoms and of the organism. It was superior to another antibiotic syntomycin: it was also considered superior to streptomycin and aureomycin used in previous years. It was also considered equally effective in the present series in cases where no pathogenic organisms were isolated.

A. B. Christie

TUBERCULOSIS

SOUTH PACIFIC COMMISSION. Noumea, New Caledonia. **Tuberculosis Conference (Pago Pago, American Samoa, 10–21 November, 1958). [i] Background Papers.** Numerous mimeographed pp., illustrated. [Numerous refs.] 1958, Nov. **[ii] A Selected List of Bibliographical References (with Annotations and Notes).** SPC-TBC/T.2/1. 52 mimeographed pp. 1958, Sept.

The South Pacific Commission was set up in 1947 by the 6 Governments administering island territories in the South Pacific *viz.* Australia, France, the Netherlands, New Zealand, the United Kingdom and the United States of America. Its aim is the well-being of the people of the islands.

A tuberculosis conference was held in American Samoa in November 1958 and its proceedings have already been the subject of a notice in the *Bulletin* [1959, v. 34, 424]. The volumes now being reviewed contain papers connected with the conference. In the first are general papers prepared by consultants and participants and "background" papers dealing in detail with the tuberculosis situation in the various territories. The second volume contains reviews of useful books on tuberculosis and a bibliography of references to tuberculosis in the region. It was compiled by the staff of the Commission and is a valuable source book both for those working in the area and for other students of tuberculosis. It will not be mentioned further here.

In the general section of the first volume E. W. ABRAHAMS (Australia), spoke on *The Aims and Purposes of a Community Programme in Tuberculosis.* The major aim is the elimination of the disease by the elimination of the tubercle bacillus but if this is achieved the resulting community will have to be protected against reinfection from without as Pacific islanders, unlike Europeans, do not yet possess genetically acquired resistance. A combination of quarantine and BCG vaccination would be the best measure to achieve this. There should be compulsory isolation of infectious recalcitrants. Case-finding and treatment,

tuberculin surveys and X-ray examination of reactors are also discussed.

H. H. WALKER, (Hawaii) dealt with *The Epidemiology of Tuberculosis and its Significance in Community Control.* Much is unknown about the pathogenesis of tuberculosis. For example there is no exact way of determining the inactivity of a lesion or an individual's resistance or susceptibility. There are variables both in the tubercle bacillus and its human host, and Walker is convinced that there are racial differences in reaction to infection. Sex and age differences in morbidity and mortality need to be studied in any community. In all probability the decline in tuberculosis has resulted from progressive increase in human resistance due to the influence of selective mortality and to improved living standards.

F. HEAF, (Great Britain) gave much sound and practical advice on *Diagnosis, Case Management* and *Contact Control.* His papers contain many valuable remarks such as that "The microscope has always been a powerful agent in diagnosis, particularly in the tropics and although in chest diseases it has been to some extent overshadowed by X-rays it still remains the first line of investigation". There is a danger of relying too much on skiagrams and neglecting other clinical methods. Bronchography is unpleasant for the patient and should not be undertaken unnecessarily. Its value increases with the experience of the operator.

In case management that which is good for the community is generally good for the individual. Domiciliary treatment will have to be provided in all countries but it should follow a short intensive course of chemotherapy in an institution. The creation of plenty of inexpensive hospital beds with effective preventive measures is the best basis of tuberculosis control.

Contact control is an essential part of a tuberculosis service. It comprises notification and continual search for infection by sputum examination, X-ray examination and tuberculin testing. The last can be applied cheaply to masses of children and may reveal hidden sources of infection in their environment.

R. MANDE (France), dealt with prophylaxis. The classical measures of tuberculosis control yield excellent results if the incidence of the disease is low, the health services well equipped, the population disciplined and hospital and treatment facilities adequate. Control is, however, very difficult when the above conditions do not exist.

Preventive immunization aims at raising resistance so that tuberculosis does not develop even in the presence of tubercle bacilli. BCG vaccination is based on the undoubted existence of acquired immunity to tuberculosis that follows primary infection. The technique of vaccination is described and some classical examples of its efficacy given.

Mande then goes on to deal with chemoprophylaxis. He gives evidence of the value of isoniazid combined with PAS in preventing the development of complications after primary infection of children. Another method of chemoprophylaxis is to use isoniazid for the temporary protection of a limited group against infection by a known infector or to protect a whole population against infection from any source.

The remainder of the volume is taken up with papers on the actual tuberculosis situation in the South Pacific area. There is a great amount of detail which is naturally of most interest to those working in the area. The findings are recapitulated as follows:

1. Higher susceptibility to tuberculosis in all age-groups compared with Caucasians living in more highly developed countries in the temperate zone.
2. Considerable frequency of acute highly disseminated, exudative or evolutive forms of pulmonary tuberculosis.
3. Frequent basal localizations.

The historical and cultural background is well described in some of the papers. *H. G. Calwell*

SOMAN, S. D. **Problems of Tuberculosis in Pregnancy.** *J. Ass. Med. Women in India.* 1959, Feb., v. 47, No. 1, 28–37, 2 charts. [11 refs.]

Returns from the BCG Centre in Bombay show that in the period 1951–5 the tuberculin reactor rate in males aged 25 and over was 97·9% and in females 94·4%. So far as the incidence of infection as determined by the tuberculin test is concerned, it is more or less the same in both sexes.

The death-rate from tuberculosis is, however, consistently higher in females aged 15–30 years than in males of the same age-group and neither in Bombay nor elsewhere is there a general environmental factor responsible for the discrepancy. The problem therefore is whether this peculiar distribution of high mortality of females aged 15–30 years is due to their sex and whether pregnancy is an additional hazard in tuberculous women of child-bearing age.

The literature on the subject is reviewed, and according to the author no specific effect of pregnancy upon resistance is known at present nor is there evidence of the disease process being stimulated by metabolic changes of pregnancy or by sex or other hormones. Nevertheless there is enough epidemiological evidence of the deleterious effect of pregnancy on tuberculosis.

Evidence is quoted that pelvic tuberculosis occurs as an early manifestation of primary disease. It is a greater risk if primary infection takes place during adolescence, and BCG vaccination is advised before that age is reached.

Soman remarks that if all tuberculosis deaths in young females associated with pregnancy within one year previously were excluded from the total tuberculosis deaths in this age period there would be much less difference between the mortality rates in young females and young males. She does not believe that reliance on therapy alone will reduce the death rate in females in the childbearing period. *H. G. Calwell*

LEVY, D. & RUSSELL, W. F., Jr. **The Effect of Topical Hydrocortisone Acetate Ointment at the Site of Intracutaneous Tuberculin Reaction.** *Amer. Rev. Tuberculosis.* 1959, May, v. 79, No. 5, 666–8.

Local necrosis of the skin, itching, pain and the unsightly nature of a markedly positive Mantoux reaction are undesirable side-effects of no diagnostic significance which it is desirable to avoid.

There is general agreement that the corticosteroids

exert an inhibitory action, either total or partial, on reactions of hypersensitivity, and the object of this paper is to report preliminary observations on the effect of the local application of a hydrocortisone ointment at the site of a tuberculin injection.

The tuberculin used was a phenol-soluble fraction of OT previously adjusted to be equal to OT 1 : 1,000 solution (10 TU/0·1 ml.). A group of 26 patients were injected with 0·1 ml. of 1 : 2,000 dilution of the phenol-soluble fraction on each forearm. All but 2 had proved pulmonary tuberculosis and were known to be tuberculin reactors. Immediately after the injection hydrocortisone acetate ointment (1%) was rubbed into both injection sites for 2 minutes when patients were permitted to remove what was left of the ointment but were asked not to wash the injection site for at least 1 hour or more.

An additional group of 12 patients were injected as above except that the ointment was not applied at 1 of the sites until 24 hours after the injection; in 3 patients the ointment was not applied until after 48 hours, and finally in 3 patients the ointment was applied on 1 arm 24 hours after injection of OT whereas on the other rose water ointment was used. It caused no change on the size or form of the tuberculin reaction.

Examination of the reactions of patients to whom the hydrocortisone ointment was applied at the time of injection showed that it produced a mild aggravation of the reaction in the majority. It did not influence the marked reactions nor did it prevent a severe reaction with necrosis in 1 patient. The negative reaction in 2 patients was not influenced by the ointment.

When the ointment was applied to the site of the tuberculin reaction after 24 hours a definite reduction was noted in those with marked or severe reactions. 6 of 12 patients complained of itching and 2 of pain on the control side only. 1 complained of itching at the site with the ointment, which continued for 12 hours after application and then receded. The itching at the control site persisted. The patient with the most severe reaction had pain in both arms.

The application of ointment 48 hours after the tuberculin injection did not alter significantly the size of induration observed at 72 and 96 hours after the test in patients in this group who had moderate reactions at the control site. In 1 patient the reaction progressed to a slough on the control side on the third day but remained stationary on the treated side.

These preliminary studies suggest a method of preventing unnecessarily severe reactions and minimizing undesirable side-effects of tuberculin hypersensitivity. A statistically controlled trial of the method requires to be made in a large number of subjects.

H. G. Calwell

HARRIS, L. C. **Generalized Tuberculous Adenitis in Bantu Children in South Africa.** *Pediatrics.* Springfield, Ill. 1959, May, v. 23, No. 5, 935–44, 3 figs. [10 refs.]

The author describes 15 cases of generalized tuberculous adenitis in Bantu children in South Africa aged 11 months to 15 years.

The patients had cervical adenitis and involvement of at least one other group of glands (excluding intrathoracic glands) and some times of more than 2 groups. The cervical glands were enlarged on both sides in all except one, and in most cases the enlargement was very marked. The condition is well illustrated in the photographs in the text.

The criteria of diagnosis included biopsy, direct finding of tubercle bacilli in a gland and in the cerebrospinal fluid respectively in 2 cases, the concurrence of miliary disease of the lung in 1 and the demonstration of calcification in cervical and intrathoracic glands in 1.

All were Mantoux reactors but it is noted that 1 patient who had had measles recently did not react on admission but did so later, and another who was a reactor displayed anergy later on the development of miliary disease. The clinical findings are given in tabular form and in addition there are notes of 8 patients.

The glands affected were especially the superficial cervical, cervical and axillary groups but inguinal, hilar, paratracheal and intra-abdominal glands were also involved. In 3 patients the primary focus was shown radiographically in the lungs; there was no evidence of multiple primary foci.

On clinical grounds the disease could be divided into acute and chronic forms. Patients with histories of 6 months or less and without demonstrable calcification of glands on X-ray examination were regarded as having acute disease; those with longer histories or with demonstrable calcification were considered to have chronic disease. 6 children in the series had the acute form. Such patients are generally more ill than the others. They are usually wasted and show the hair, but not the skin, changes of kwashiorkor. Low-grade or, less often, high fever and some degree of anaemia are common. The cervical glands may be large enough to cause stridor. In most cases the glands are not fluctuant, and sinuses are not commonly present. In the acute stage the glands are matted, relatively fixed and of only moderately firm consistency.

All patients were treated with isoniazid, 10–20 mgm./kgm. and PAS 0·5 gm./kgm. daily. Streptomycin 1·0 gm. daily was given to 2 patients but is not considered necessary in uncomplicated cases. There was marked improvement in 3, moderate improvement in 6, slight improvement in 1 and 3 did not improve. Suppuration of glands occurred in 4, and 2 patients died both of whom had miliary disease. When suppuration occurs surgical drainage and irrigation with a solution of streptokinase and streptodornase may be necessary.

The condition appears to result from lymphohaematogenous spread and it appears to be commoner among Negroes than whites. *H. G. Calwell*

SILWER, H. & OSCARSSON, P. N. **Incidence and Coincidence of Diabetes Mellitus and Pulmonary Tuberculosis in a Swedish County.** *Acta Med. Scandinavica.* 1958, v. 161, Suppl. 335, 48 pp., 3 figs. [Numerous refs.]

Part I. Incidence of Diabetes Mellitus in a Swedish County

By searching hospital records and by sending questionnaires to all general practitioners who might have treated diabetics resident in the county of Kristianstad, 1,326 cases were found on March 15, 1954 in a population of just over one-quarter of a million. The corresponding prevalence rates, which probably underestimate the true frequencies, were 4·6 and 5·7 per 1,000 men and women respectively. The prevalence was low below 40 years of age, and showed a slight male excess. Above this age rates rose steeply to peaks of 22 and 16 per 1,000 for women and men of 70–79 years. At older ages the urban prevalence was slightly greater than the rural. The distribution of cases by age at diagnosis followed a pattern similar to that for prevalence but shifted about 10 years earlier. In the youngest patients the disease was in general more severe and nearly all were receiving insulin, while in the oldest about 60% were receiving it. Of the total 13% had had coma or precoma on at least one occasion, while just under 10% had a pronounced tendency to acidosis.

Part II Incidence of Pulmonary Tuberculosis among Diabetics

The group of 1,326 revealed in the previous study was used in a cross-sectional study to estimate the prevalence of pulmonary tuberculosis among them. Such a study does not give information on the course of the disease in diabetics, excluding in particular those who have died. Radiological examination of 1,270 diabetics, 96% of the total, revealed 46 with pulmonary tuberculosis, a prevalence of 3·6% which was far greater than that of 0·88% based on the dispensary records for the county as a whole after a mass X-ray survey. This preponderance was seen in each age-group except 0–9 years, where the number of diabetics was too small to provide a reasonable estimate. Conversely, among both tuberculous patients registered with the dispensaries and those admitted to the County Sanatorium the incidence of diabetes was found to be greater than in the survey of the whole county reported above. Pulmonary tuberculosis was twice as prevalent in diabetics under 50 years as in those over this age, and was about 4 times commoner in patients with severe than in those with mild diabetes, being particularly common in those with a history of coma or tendency to acidosis. The prevalence also increased with the duration of diabetes. In only 3 of the 46 patients was the pulmonary lesion discovered before the diabetes. It is concluded that all diabetics should be examined regularly by chest X-ray because of the high risk of coexisting pulmonary tuberculosis. *J. Knowelden*

COURTOIS, R., VANROUX, R. & ANDRÉ-COURTOIS, M. L. Antibiotiques et tuberculose pulmonaire. Chimiothérapie de très longue durée. Chimioprophylaxie. Médications nouvelles. [**Antibiotics and Pulmonary Tuberculosis. Prolonged Chemotherapy. Chemoprophylaxis. New Drugs**] *Bruxelles-Méd.* 1959, May 17 & 24, v. 39, Nos. 20 & 21, 689–98 & 719–30. [49 refs.]

This is a long review of the literature on the chemotherapy of pulmonary tuberculosis and on chemoprophylaxis. Much of the work mentioned is already familiar to readers of this *Bulletin*.

Many workers have found that the 6th month of treatment with a combination of the standard antituberculous drugs is the most critical as after that time the drugs appear to lose their efficacy.

At the end of 6 months the patient may be well with a negative sputum and radiological evidence of resolution of the disease, or he may appear well, have a negative sputum but radiological evidence that the lesions are still unstable. In the first case chemotherapy should be continued to consolidate the cure and in the second also it should be continued without surgical intervention. If, however, there is complete failure of intensive chemotherapy, recourse should be had to collapse-treatment or resection. The total duration of chemotherapy is the subject of argument. Some advise 8 months or less and others continue indefinitely.

The risk of the emergence of drug-resistant strains of tubercle bacilli increases with the duration of chemotherapy. The majority of patients treated cease to expectorate bacilli which nevertheless may continue to survive in the tissues because the drugs cannot reach them or do not affect them as they are in a physiological state of " rest ".

It is unusual to find complete resistance to all 3 standard drugs in cultures of bacilli obtained from sputum or specimens of resected tissue. There is evidence that resistant bacilli have reduced vitality and the danger to the patient is from sensitive bacilli. The prolongation of chemotherapy is therefore rational.

Tubercle bacilli which resist a concentration of 50 μgm./cc. of isoniazid in culture do not produce tuberculosis in guineapigs, monkeys, young pigs or gerbils but remain pathogenic for mice and hamsters. In order to be conclusive such experiments require strains selected from cultures for bacilli classified as resistant after culture directly from sputum or tissues may also contain some sensitive organisms which will cause delayed lesions. The loss of virulence of isoniazid-resistant bacilli is proportional to their degree of catalase-negativity. Isoniazid-resistance, diminished virulence and catalase-negativity are generally regarded as enduring and inheritable characteristics.

The importance of isoniazid-resistance is 2-fold affecting the patient himself and his contacts. Nearly all clinicians are agreed that the disease continues to get worse in the stage of resistance of the bacillus but it is not yet possible to assess the danger to contacts. Cases of proved infection by isoniazid-resistant organisms are rare but there is no justification for regarding a patient who is expectorating resistant bacilli as non-infectious. Some sensitive bacilli probably persist and even among the resistant bacilli some may be catalase-positive with retained virulence.

Prophylactic chemotherapy, by which is meant the administration of drugs to those infected recently or found to have apparently inactive tuberculous lesions in order to prevent the extension of the disease, is principally indicated in the stage of adenopathy of the primary infection and while not influencing the primary complex may prevent the onset of meningitis or miliary disease for example. Trials of the method are in progress. Prophylactic treatment should last for 4–8 months (12 months in children) or for a longer period. The regime of choice is isoniazid combined with PAS.

Suitable candidates are recently infected children, pregnant women, diabetics or patients undergoing prolonged treatment with cortisone. *H. G. Calwell*

KAWASHIMA, H., MATSUOKA, I., OBA, M. & WAKIZAKA, H. **[A Lethal Case due to Cholemia developed while applying Sodium P-Aminosalicylic Acid (PAS) Therapy]** *Igaku Kenkyu.* Fukuoka. 1958, Dec., v. 28, No. 13, 308–11. [14 refs.] [In Japanese.] English summary.

RUITER, D. & BLEIKER, M. A. De invloed van INH-toediening op recente omslag der tuberculine-gevoeligheid. **[Effect of INH Administration on Recent Conversion of Tuberculin Sensitivity]** *Nederl. Tijdschr. v. Geneesk.* 1959, May 16, v. 103, No. 20, 1059–60.

The English summary appended to the paper is as follows:—

"Ten primary school children showed a marked increase in sensitivity to a 1/2000 tuberculin solution over a period of 6 weeks. They were given daily doses of 4–5 mg. INH/kg. body weight for 2–6 months. In nine of these children a marked decrease of tuberculin sensitivity followed."

D'AGOSTINO, S. & MINGRINO, F. Porpore emorragiche e terapia antitubercolare. **[Haemorrhagic Purpura and Antituberculosis Therapy]** *Arch. Ital. Sci. Med. Trop. e Parassit.* 1959, Mar., v. 40, No. 3, 169–78. [37 refs.]

The English summary appended to the paper is as follows:—

"Report of a case with anaphylactoid purpura probably due to isoniazid treatment.

"Hemorrhagic manifestations in tuberculous patients can to be determined either by the disease or by the antituberculous drugs. Necessity of determinant factor evaluation is stressed to establish an adequate treatment."

GUPTA, S. K. & PALMER, H. D. **Short-Term ACTH Therapy for Desensitisation against Anti-Tuberculosis Drugs.** *Brit. J. Dis. Chest.* 1959, Apr., v. 53, No. 2, 197–201. [22 refs.]

The occurrence of allergic reaction to antituberculous drugs is often a considerable drawback to treatment. The author describes 12 cases in which a short course of a combination of short and long acting corticotrophin was used in large doses. After waiting until the reaction had ceased these drugs were administered according to a scheme for 5 days. The antituberculous drugs were given at the same time. 20 units of long acting corticotrophin (L) were given on the first day; 20 units of short-acting corticotrophin (S) were given twice a day; and 20 of long-acting (L) once on the second and third days, 20 units of each on the fourth day, and 20 units of the long-acting on the fifth day. On the sixth day and onwards no corticotrophin was given but the antituberculous drugs were continued. No recurrence of the allergic reactions followed and the complications were negligible. If this work is confirmed, a useful and early method of dealing with the reactions has been discovered. *F. H. Young*

SLADE, S. E. **Ambulant Chemotherapy: a Practical Advance in the Treatment of Pulmonary Tuberculosis.** *Brit. J. Dis. Chest.* 1959, Apr., v. 53, No. 2, 193–6.

Ambulant chemotherapy is an ideal method of treatment of pulmonary tuberculosis if it is successful. The author reports on 40 patients treated in this way. He demanded sufficient intelligence to carry out the treatment, lack of toxaemia including a normal erythrocyte sedimentation rate, and absence of tubercle bacilli in the sputum. 12 of the patients were in this category, but 28 who had a positive sputum were also treated because they refused hospital treatment. The length of treatment varied from 2 to 43 months. At the end of 2 years 25 of the 28 positive cases had converted; the X-ray appearances had improved in 24 of the 40 patients. 2 patients are still under treatment, 1 patient has died, 1 still has active cavitated tuberculosis, and 1 was admitted to hospital because his mental capability was unequal to keeping up ambulant treatment. It is claimed that ambulant treatment has been successful in all the patients who were in the demanded category, and 36 of the total of 40 treated were controlled.

A table giving details of the patients is given.

F. H. Young

ANG'AWA, J. & HAYNES, W. S. **Prednisone in the Treatment of Patients with Pulmonary Tuberculosis at Port Reitz Chest Hospital, Mombasa.** *East African Med. J.* 1959, Mar., v. 36, No. 3, 147–63.

Reports on the use of steroids in conjunction with antituberculous drugs in the treatment of pulmonary tuberculosis are now appearing frequently.

This is a report on its use at the Port Reitz Hospital at Mombasa where the disease often takes a very acute form.

The first trial was on 9 acutely ill, previously untreated, patients, and 3 patients who were not responding to drug therapy. 2,110 mgm. of prednisone were given over 78 days—50 mgm. for the first 4 days, 40 mgm. for the second 48 days, and thereafter 25 mgm. daily for 10 weeks—PAS and isoniazid were given in standard doses.

In view of the satisfactory immediate results a shorter course was tried on 28 similar patients, 760 mgm. of prednisone was given in gradually reduced doses over 30 days.

As controls 15 patients with similar acute disease were studied.

Full details of results are given in 3 tables. Generally speaking the use of prednisone produced a dramatic clinical improvement and was life-saving in many cases. Sputum conversion was not materially accelerated. X-ray improvement was greater in the early stages in the treated cases, but there was not much difference on discharge, though the period of hospital treatment

could be reduced. As the main effect of the steroid therapy was in the first 30 days it was not surprising that the difference in effect between the long and short course groups was not marked.

Toxic effects were few, but withdrawal fever occurred in 33% of the long course group and 43% of the short course group. In some prednisone had to be restarted. In 10 out of 40 patients X-ray deterioration followed withdrawal; 3 patients had a very troublesome eczematous rash after stopping the prednisone.

The author concludes that in the acute type of cases which are often encountered at Mombasa prednisone is very useful in controlling severe toxaemia.

F. H. Young

TURNER, P. P. **A Severe P.A.S. Hypersensitivity Reaction controlled by Prednisolone.** *East African Med. J.* 1959, Mar., v. 36, No. 3, 164–6.

A patient is described who 3 weeks after starting treatment with PAS developed a hypersensitivity reaction, including jaundice and enlargement of liver. This disappeared when the drug was discontinued, but recurred after a test dose of 1 gm. When this reaction had subsided treatment was resumed with small doses of PAS and 30 mgm. of prednisolone daily. The dose of PAS was gradually increased and that of prednisolone reduced. No reaction occurred, and at the end of 19 days the steroid was given up and the patient continued on full doses of PAS without incident.

F. H. Young

PALEY, S. S., MIHALY, J. P., MAIS, E. L., GITTENS, S. A. & LUPINI, B. **Prednisone in the Treatment of Tuberculous Pleural Effusions.** *Amer. Rev. Tuberculosis.* 1959, Mar., v. 79, No. 3, 307–14, 6 figs. [49 refs.]

This paper starts with a useful review of the literature dealing with the use of steroids on animals and patients suffering from tuberculosis, and is accompanied by a bibliography of papers on the subject. Unfortunately it is mainly confined to papers published in the U.S.A. and even the Scottish trial [this *Bulletin*, 1958, v. 33, 111] is not mentioned. At the Harlem Hospital, New York, 26 patients suffering from pleural effusion were treated with prednisone, mainly 30 mgm. daily for 4 days, 20 mgm. for 7–14 days, and 10 mgm. for the balance of 4 weeks. In no case was a total dosage of 600 mgm. and a period of 6 weeks exceeded. With this 1 gm. of dihydrostreptomycin 3 times weekly and 300 mgm. of isoniazid were given, and it is planned to continue this for 2 years. As a preliminary, paracentesis to remove as much fluid as possible was performed, and at the conclusion of the prednisone treatment 25 mgm. of corticotropin was given.

In all 26 patients there was a remarkable immediate improvement. In 25 patients the residual fluid had disappeared in 3 to 6 weeks; 1 patient required a second paracentesis. In 1 patient a small parenchymal lesion disappeared completely in 4 months.

In 12 patients the clearing of the effusion was radiologically complete; in the remaining 14 a very slight basal pleural thickening remained. 14 of the 26 patients have been followed for 18 months and no evidence of recrudescence of disease has appeared. *F. H. Young*

GRIFFITH, A. H. **B.C.G. Vaccination by Multiple Puncture.** *Lancet.* 1959, June 6, 1170–72.

BCG vaccination is much easier to carry out by multiple puncture than by intracutaneous injection. The main disadvantage of the multiple puncture method is uncertainty of dosage, nor is it yet certain whether it can be effective and safe.

2 trials were carried out in Wales on 13-year-old schoolchildren. In the first trial non-reactor children (Heaf test) were divided into 3 groups according to their month of birth. They were vaccinated intracutaneously with 0·1 ml. of Glaxo freeze-dried vaccine (1·0 mgm./ml.) or 0·1 ml. of fresh Danish vaccine (0·75 mgm./ml.) or with Glaxo freeze-dried vaccine (50 mgm./ml.) by multiple puncture with 3 mm. penetration. The children were tuberculin tested (Heaf) 8–12 weeks after vaccination when the vaccination lesions and tuberculin reactions were measured.

All who were vaccinated intracutaneously underwent post-vaccinal tuberculin conversion but the degree of tuberculin sensitivity was greater with fresh than with dried vaccine. The fresh vaccine produced lesions on average 0·5 mm. larger than did the dried vaccine. If the diameter of the BCG lesion depends on the number of viable organisms inoculated, then it appears that the degree of post-vaccinal tuberculin sensitivity is related to the number of viable organisms inoculated.

The degree of post-vaccinal tuberculin sensitivity was less with multiple puncture than with intracutaneous vaccination, and only 83% of those vaccinated by multiple puncture underwent tuberculin conversion compared with 100% after intracutaneous vaccination with either fresh or dried vaccine. One feature of the multiple-puncture vaccination was the mildness of the vaccinal lesions produced.

In the other trial the efficacy of the multiple-puncture method with dried vaccine (20 mgm./ml., 2 mm. penetration) was compared with that of 0·1 ml. of intracutaneous Danish fresh vaccine (0·75 mgm./ml.). At the end of 12 months all the 142 children vaccinated intracutaneously were tuberculin reactors compared with 138 of 146 (95%) vaccinated by multiple puncture. At the end of 2 years 89 of those vaccinated by multiple puncture were tested and 74 (83%) were still reactors.

The discrepancy in the results of these trials may be due to difference in potency of the vaccine, in technique, in the multiple-puncture apparatus used or in the post-vaccinal tuberculin testing. In any event it is shown that the multiple-puncture method of BCG vaccination can be effective under some conditions and unsatisfactory in others. Further trial is necessary. [See also LORBER, J., this *Bulletin*, 1959, v. 34, 623.]

H. G. Calwell

PALMER, C. E., SHAW, L. W. & COMSTOCK, G. W. **Community Trials of BCG Vaccination.** *Amer. Rev. Tuberculosis.* 1958, June, v. 77, No. 6, 877–907, 4 figs. [50 refs.]

This is a progress report on 2 controlled community trials of BCG vaccination against tuberculosis, undertaken

in Puerto Rico and in the states of Georgia and Alabama, as part of the Tuberculosis Programme of the U.S. Public Health Service. The trials began in 1949 and 1950 respectively, and the present results relate to the first 6 to 7 years of follow-up observation. Both trials incorporated a system of random allocation to the vaccinated and the unvaccinated control groups, for those found to be non-reactors to tuberculin. Tuberculin reactors, though not considered eligible for vaccination, were included in both study populations to permit a determination of how much of the total amount of tuberculosis could have been prevented by vaccination.

In Puerto Rico 191,800 children aged from 1 to 18 years (about 18% of the island population of these ages) were skin-tested with 1 tuberculin unit (TU) of PPD (RT 19–20–21) and, if negative (5 mm. induration or less after 72 hours), with 10 TU. Those negative to 10 TU, numbering 109,600, were eligible for vaccination, but 31,600 refused. Of the remainder, 50,600 were vaccinated and 27,300 were kept unvaccinated as controls; all these, whether vaccinated or not, were also skin-tested with 100 TU. The allocation depended on the year of birth, and was designed to yield about twice as many vaccinated persons as controls. The BCG vaccine (0·1 mgm./ml.) was prepared by Dr. K. Birkhaug at the New York State Department of Health, and was given by intracutaneous injection in the left deltoid area. The tuberculin testing and vaccination were done by teams of specially instructed public health nurses; there was no roentgenographic screening of the participants on entry.

In Georgia and Alabama 64,100 persons, representing about one-half of the general population aged 5 years and upwards in the counties of Muscogee and Russell, had a 70 mm. photofluorogram taken and were skin-tested with 5 TU of the same PPD; those negative (4 mm. induration or less after 72 hours), numbering 34,800, were eligible for vaccination, and few refused. They were allocated almost equally, according to year of birth, to a vaccinated group (16,900) and an unvaccinated control group (17,900). The BCG vaccine was obtained from Dr. S. R. Rosenthal of the Research Foundation in Chicago, and was given by a multiple puncture technique in the left deltoid area by specially trained nurses. The study population was confined to those whose photofluorogram on entry was classified as normal by 2 readers.

As a precaution against bias, no systematic follow-up examinations of the local vaccinal lesions were made in either trial, and information on post-vaccinal tuberculin sensitivity was only obtained incidentally in the course of later sample surveys of the general population; in Puerto Rico 89% of the vaccinated persons were positive to 10 TU (6 mm. induration or more) 1–2 years after vaccination, and in Muscogee-Russell 54% of the vaccinated persons were positive to 5 TU (5 mm. induration or more) 2 years after vaccination. In each trial the follow-up was deliberately based upon the established reporting systems for cases of and deaths from tuberculosis in the trial areas, as being sufficient for the purposes of the study, and also more likely to yield unbiased information than systematic periodic examinations. In Puerto Rico any person reported as having tuberculosis or as dying of the disease was accepted as a case; in line with the policy of avoiding bias "no attempt was made to verify the accuracy of the diagnosis . . . even though errors undoubtedly occurred". In Muscogee-Russell, for the same reason, the films for all persons ever suspected of having tuberculosis were submitted for an independent diagnosis to a reviewer who had never been associated with the study. No account is taken in the present report of the persons who moved away from the trial areas during the follow-up period.

Comparisons of the controls and vaccinated in each area indicate that the groups were similar in their race, sex and age composition, in their urban/rural distribution (in Puerto Rico) and in the prevalence of low-grade initial tuberculin sensitivity.

In the Puerto Rico trial 1,149 cases of tuberculosis would have been expected in the absence of vaccination, comprising 856 which occurred among the tuberculin reactors who were ineligible for vaccination, plus 293, which represents the estimated number among the non-reactors if none of them had been vaccinated. Thus 293 (25%) of the potential total of 1,149 cases would have been subject to the direct effect of vaccination. There were 73 cases among 27,338 controls and 93 among 50,634 vaccinated persons, representing annual incidences of 43·2 and 29·8 per 100,000 respectively; the percentage reduction in tuberculosis among the vaccinated was thus 30·9%, which is statistically significant at the 1% level. The reduction in the total number of cases which could have been accomplished by vaccinating all the non-reactors is estimated from this finding as 91 cases, which is 7·9% of the total of 1,149.

In the Muscogee-Russell trial, 216 cases would have been expected in the absence of vaccination, 161 among the reactors, and 55 (25%) among the non-reactors; there were 28 cases among 17,854 controls and 17 among 16,913 vaccinated persons, giving annual incidences of 22·4 and 14·4 per 100,000 respectively; the apparent reduction in tuberculosis among the vaccinated was 35·9%, but this difference could readily have arisen by chance. If all the non-reactors had been vaccinated 20 cases might have been prevented, which represents a reduction of 9·3% in the total of 216 expected cases.

In the Puerto Rico trial, reactors had more extensive disease than non-reactors; the type of disease among controls did not differ significantly from that among vaccinated persons. In the Muscogee-Russell trial there were no statistically significant differences in the distribution of the kinds of cases among reactors, controls and vaccinated.

Comparison is made of the findings of these 2 trials with those of the British Medical Research Council trial [this *Bulletin*, 1956, v. 31, 621]. All 3 trials agree in showing that tuberculin reactors are subject to high tuberculosis case rates. However, in the British trial vaccination (with Danish BCG) was reported to be more than 80% effective, compared with a little more than 30% in the Puerto Rico and Muscogee-Russell trials. Vaccination could have decreased the total number of cases in the British study population by "more than 40 per cent" [the figure given in the British reports in 55%], compared with less than 10% in the Public

Health Service trials. The authors conclude that reconciliation of these differences does not seem possible. They find it difficult to accept or reject differences in the immunizing potency of the vaccines as a cause of significant differences in the observed effectiveness of vaccination. They claim "serious defects" in the design and execution of the 3 trials, largely due to the lack of an adequate placebo for the controls. They are critical of the British trial because the subjects may have been frequently reminded of their tuberculin and vaccination status during the course of the trial, and because the team physicians also had access to this information, and decided which cases would be reported to the independent reviewer as possible tuberculosis. "It is difficult to see how assurance can be given that bias was avoided in the selection of cases submitted to the reviewer." [Further reports on the British trial will be awaited with interest.]

A further difference between the British and the Public Health Service trials is that low-grade tuberculin sensitivity is highly prevalent in the Puerto Rico and Muscogee-Russell populations, and less common in the British study population. Moreover persons with low-grade sensitivity were included among vaccinated persons and controls in the Public Health Service trials, but excluded from both categories in the British trial. The authors conclude that the evidence is at present insufficient to decide whether these differences might account for the different results in the British and Public Health Service trials. It may, however, be injudicious to assume that results obtained in one situation are applicable elsewhere.

In discussing their findings, the authors are impressed first by the much higher risk of tuberculosis developing among the reactors than the non-reactors, apparently because the opportunities for new infection of non-reactors have become relatively infrequent, and not because of any increase in the rates among reactors, in recent decades. The usefulness of vaccination will depend upon the infection rate among the non-reactors; if, in the present trials, the infection rates had been lower, vaccination would have been even less useful in reducing the total amount of tuberculosis. With falling infection rates, a point will be reached in any population when the disadvantages of vaccination outweigh the advantages.

The really significant penalty of vaccination is its interference with the interpretation of the tuberculin reaction; the tuberculin sensitivity conferred by vaccination makes it impossible to identify the occasional persons who become infected, or to keep those naturally infected under surveillance (or perhaps to give them prophylactic treatment).

The authors conclude that vaccination is not indicated on an extensive scale in the U.S.A., and perhaps not even among special groups such as nurses, medical students or laboratory workers unless the present and probable future risk of infection for the group has been ascertained. *Ian Sutherland*

ANDERSON, A. S. *et al.* **The Case against B.C.G.** *Brit. Med. J.* 1959, June 6, 1423–30. [48 refs.]

According to its 17 authors (all located in the U.S.A.) the main purpose of this paper is to call attention to the natural history of tuberculosis and the factors which seem to have been most important in the changing tuberculosis scene. The subsidiary purpose may be guessed from the title.

In 1930 the number of newly reported cases of tuberculosis in the United States was almost 125,000, in 1954 100,540, and in 1956 almost 69,000—a fall of 44·9%. Moreover the proportion of cases diagnosed because of symptoms had decreased. The tuberculosis death-rate was 70·2 per 100,000 in 1930 and 8·4 in 1956, and the improvement was most marked in children and young adults.

It is estimated that there are some 56,000,000 infected persons and these, and those whom they infect will continue to provide the new cases of tuberculosis but the attack rate is falling and tuberculous infection in young children has become relatively rare in rural areas. In an unnamed city the reactor rate in school-children was under 4% in 1954 [but this is a very favourable rate even for the United States and much higher rates obtain in some areas].

Veterinarians in Canada and the United States tested BCG vaccination in cattle some 30 years ago and found it useless. The World Health Organization has recognized its incompatibility with the use of the tuberculin test as a basis of control of tuberculosis in cattle where the test is used to detect reactors so that they may be removed from the herd and slaughtered. [The relevance of this to BCG vaccination of human beings is a little obscure to the reviewer.]

The authors believe that tuberculin sensitivity is specific for tuberculosis. [No mention is made of the occurrence in various parts of the world of low-grade sensitivity in human beings constituting a non-specific response, whose cause is not known. Furthermore it is well known that veterinarians have often failed to detect any evidence (macroscopic or microscopic) of tuberculosis in the bodies of slaughtered reactor animals.]

A primary tuberculous infection whether due to natural tubercle bacilli or to BCG follows the same course with reference to distribution and the formation of the primary complex. The authors do not think it reasonable to classify them differently, and one of them (MYERS, J. A.) is quoted as having said in 1935 that the immediate prognosis of tuberculosis of the first infection type in children and young adults is excellent. This is supported by his finding in 1957 that of 2,266 young adults who underwent tuberculin conversion only 5 developed clinical tuberculosis although there was a demonstrable primary pulmonary complex in 54. 67 developed pleural effusion of whom 9 developed tuberculosis later. None died of tuberculosis.

The immediate danger of natural primary infection should not be overemphasized. In a series of 813 infected children aged 0–5 years "only 11 developed acute, fatal reinfection forms of disease and another 11 later developed chronic reinfection type of lesion . . .". In another series 137 (4·6%) of 2,979 reactors developed chronic tuberculosis. The authors' comment on these findings is that if BCG had been used it might have been given the credit for protecting the 3,651 children who in fact did not develop tuberculosis. [The reviewer's comment is that if BCG had

been used many of the 159 children would have been saved from death and illness.]

The long-term hazard of primary infection is stressed, and emphasis is put on the need to concentrate on reactors rather than non-reactors.

The authors do not admit that there are "unavoidably exposed groups" including students of medicine and nursing. Such exposure to tuberculous infection is a reflection on the administration and professional staff of any hospital or nursing school. Myers has got rid of the danger by introducing rigid contagious-disease technique where students come into contact with known cases of contagious tuberculosis. In addition patient-admission examinations for tuberculosis, and pre-employment examinations of all personnel with subsequent periodic examinations were instituted.

Some of the reported trials of BCG vaccination such as that of J. D. ARONSON *et al.* [this *Bulletin*, 1952, v. 27, 1018; 1958, v. 33, 943] and that of the Medical Research Council [this *Bulletin*, 1956, v. 31, 621] are discounted because of alleged failure to differentiate between harmless primary pulmonary infiltrates and tuberculosis Another ground of criticism is that no trial has gone on long enough.

The possibility of mutation of BCG towards virulence either in culture or in the human body is discussed. Nothing new is said.

[These 17 authors have not produced a single new idea or quoted any personal experience of BCG vaccination. The paper is a review of some of the literature chosen with a bias. This is not to decry much valuable work in tuberculosis control that some of them have accomplished in the United States.] *H. G. Calwell*

LORBER, J. & MENNEER, Peggy C. **Long-Term Effectiveness of B.C.G. Vaccination of Infants in Close Contact with Infectious Tuberculosis.** *Brit. Med. J.* 1959, June 6, 1430–33, 3 figs.

In order to get information about the long-term effectiveness of BCG vaccination in contacts of tuberculous persons the authors have followed up 267 contact children in Sheffield who were under the age of 2 years when vaccinated with BCG.

The children were isolated from the known infector before and after vaccination as required, and they were tested with tuberculin before and after vaccination except that newborn infants were vaccinated without a pre-vaccinal test. All were permitted to resume contact with the patient after tuberculin conversion no matter what the state of the disease.

Clinic supervision of the vaccinated children was maintained, and at the end of the 3rd year and annually thereafter they were X-rayed and tuberculin tested.

It was found possible in a period of 1957–8 to trace 261 of the 267 children who had been vaccinated 5 or more years earlier and to see and examine 248 (92·9%). None had died of tuberculosis, 3 had died of other causes, 10 (3·7%) who were known to be alive and well refused examination, and 6 (2·2%) were untraced.

Of the 248 children tested with tuberculin 243 (98%) were reactors, 4 were non-reactors and 1 failed to attend for reading. The non-reactors were re-vaccinated and the BCG lesion developed normally.

X-ray examination was complete in 235 children; no abnormality was seen in 232 (98·8%) and calcified lesions were seen in 3 (1·2%). One of these children never had any symptoms suggestive of tuberculosis or respiratory disease, and his pulmonary lesion was a minute calcified focus; the other 2 had minor clinical symptoms associated with tuberculous lung lesions which had healed by calcification. Neither required antituberculous chemotherapy. The one child had lived in contact with a sputum-positive grandfather and the other with her tuberculous mother and grandmother. Case histories are given in full.

"As there were no comparable controls it cannot be shown conclusively that B.C.G. vaccination prevented tuberculosis in this group of infants. Nevertheless the results are highly suggestive that this, in fact, was the case." *H. G. Calwell*

ELLMAN, P. & ANDREWS, L. G. **"B.C.G. Sarcoidosis".** *Brit. Med. J.* 1959, June 6, 1433–5, 2 figs. [31 refs.]

The aetiology of sarcoidosis is uncertain. A large school of thought believes it to be a group of granulomatous diseases of known cause—for example, tuberculosis, histoplasmosis, brucellosis, berylliosis—or to be idiopathic.

The occurrence of sarcoidosis in persons previously vaccinated with BCG has been recorded [see for example this *Bulletin*, 1958, v. 33, 225], and the term "B.C.G. sarcoidosis" has been applied to these cases, of which another is reported in this paper.

A girl aged 14 years who failed to react to the Mantoux test with 100 TU was vaccinated with BCG. Tuberculin conversion followed (10 mm. to Mantoux 3 TU). She reacted to 3 TU (7 mm.) 3 years after vaccination but failed so to react 15 months later although she reacted to 100 TU with induration of 12 mm. In the 6th year after vaccination she reacted to 3 TU with 14 mm. of induration. Annual X-ray examination of the chest revealed no abnormality.

In the 7th year after vaccination she failed to react to the Mantoux test with 3 TU, and the skiagram showed reticular mottling of both lungs. 2 months later she failed to react to 10 and 100 TU and the mottling was more extensive. She was admitted to hospital. There were no symptoms of illness. Small cervical and scalene lymph nodes were palpable, the liver edge was felt 1 fingerbreadth below the costal margin, and the spleen was just palpable. Details of blood cytology and chemistry are given. Acid-fast bacilli could not be isolated. Liver biopsy showed changes compatible with sarcoidosis *viz.* multiple granulomata showing giant cell formation without caseation or demonstrable acid-fast bacilli. The Kveim test was negative.

No active treatment was given and the girl returned to work. Radiographic resolution was complete within a year and she regained tuberculin sensitivity.

The literature on the occurrence of sarcoidosis in persons vaccinated with BCG is reviewed. Sarcoidosis and vaccination may be coincidental but there is evidence that the incidence of sarcoidosis as compared

with tuberculosis is higher in vaccinated than in unvaccinated groups.

The authors consider it unlikely that the vaccination precipitates sarcoidosis in view of the long interval of time between them, and it may be that without vaccination these persons would have developed tuberculosis and that the vaccination modifies the course of the infection to sarcoidosis. *H. G. Calwell*

LE CHUITON, F., CHAMBRY, J. L. G. & DAOULAS, R. J. Essai d'interprétation pouvant expliquer l'atténuation des réactions cutanées à la tuberculine, survenant dans certains cas, au cours de la vaccination au BCG par la méthode de De Assis. [**Weak Tuberculin Reactions Following "Concomitant" BCG Vaccination**] *Bull. Acad. Nat. Méd.* 1959, v. 143, Nos. 11/12, 266–8.

DE ASSIS [this *Bulletin*, 1954, v. 29, 603] described his method of "concurrent" or "concomitant" BCG vaccination in which infants are given repeated large doses of vaccine by mouth. He and others found that repetition of the doses of vaccine have the effect of reducing or abolishing the tuberculin sensitivity which followed the first dose or had been naturally present before vaccination.

The question arises whether this finding invalidates the classical theory of CALMETTE and others that immunity against tuberculosis cannot exist in the absence of tuberculin sensitivity. The authors do not think that it is necessary to abandon Calmette's theory and they propose a reconciling explanation.

Their first step is to outline the chemical composition of the tubercle bacillus and the antigenic properties of its constituents after which they go on to interpret the phenomena accompanying the method of vaccination described.

If in the course of repeated ingestion of BCG vaccine tuberculin sensitivity is seen to be diminished or disappears while the BCG skin test remains positive it is because immunity is so strong that it masks sensitivity. This is comparable with what is seen with a negative Schick reaction when the immunized organism contains sufficient antibody to neutralize diphtheria toxin.

Failure to detect tuberculin sensitivity does not imply its regression or disappearance; rather it cannot manifest itself because the immunizing antibodies have neutralized the antigen.

On the contrary if the BCG test remains positive it is chiefly because immunity to the chemical substances contained in the bacilli is not yet sufficient to neutralize them or because certain allergens in the bacilli are more plentiful than in tuberculin alone.

It is possible that if the ingestion of BCG were continued for a longer period a degree of immunity would be achieved which would result in the BCG test becoming negative also. *H. G. Calwell*

VENEREAL DISEASES

HARRISON, L. W. **The Origin of Syphilis.** *Brit. J. Venereal Dis.* 1959, Mar., v. 35, No. 1, 1–7. [28 refs.]

Col. Harrison needs no introduction; there can be few living who know more about syphilis than he.

In this article he presents a series of closely reasoned arguments to show that syphilis was introduced into Europe by Christopher Columbus and his followers late in the 15th century.

It is admitted that syphilitic bones dating before A.D. 1300 have been found in North and South America and it seems probable too that the mutation of *Treponema pallidum* occurred in America.

The author proceeds to demolish one by one the arguments that syphilis existed in Europe from the most ancient times; syphilitic rashes are easily confused with other dermatoses, aneurysms are not all syphilitic, gumma in bones may simulate arthritis deformans and so on.

Moreover, some of the edicts against syphilitics in France have been misquoted or wrongly dated by those who cited them, but evidence for or against this cannot be quoted in full.

All who are interested in the history of syphilis should study this scholarly article and they will then realize the vast amount of time and labour which have gone into its compilation. *T. E. Osmond*

FIUMARA, N. J., APPEL, B., HILL, W. & MESCON, H. **Venereal Diseases Today.** *New England J. of Med.* 1959, April 23 & 30, v. 260, Nos. 17 & 18, 863–8 & 917–24, 1 fig. [57 refs.]

5 venereal diseases are recognized *i.e.* syphilis, gonorrhoea, chancroid, lymphogranuloma venereum and granuloma inguinale, but non-gonococcal urethritis and trichomoniasis are not included in these articles though they probably present the most difficult problems in VD clinics in England today.

This communication is divided into 2 parts; the first deals with public health progress in the U.S.A., the effect of the introduction of penicillin into treatment, the trends of syphilis and gonorrhoea, mass blood testing, education of the public and contact investigation. This last seems to have received less attention than it deserves and the idea that VD has been conquered is scouted; the great difficulty is that more and more VD is being treated by general practitioners who have neither the time nor the facilities for reporting cases and tracing contacts.

The second part deals with the history, diagnosis and treatment of syphilis and gonorrhoea; one important fact stands out *i.e.* the very large numbers of teenagers who contract these diseases. Most of this section appears to be much the same as can be found in any text book on the subject but mention is made of several tests which may in the future be helpful *e.g.* the rapid plasma reagin test, fluorescein-tagged antibody tests and skin tests. *T. E. Osmond*

BEERMAN, H., NICHOLAS, L., SCHAMBERG, I. L. & GREENBERG, M. S., with the collaboration of T. GUTHE & C. J. HACKETT. **Syphilis. Review of the Recent Literature.** *Arch. Intern. Med.* 1959, Mar. & Apr., v. 103, Nos. 3 & 4, 460–83; 621–43. [243 refs.]

CANNEFAX, G. R. & GARSON, W. **The Demonstration of a Common Antigen in Reiter's Treponeme and Virulent** *Treponema pallidum*. *J. Immunology.* 1959, Mar., v. 82, No. 3, 198–200.

In order to confirm the hypothesis that a group-specific antigen exists in Reiter's spirochaete and virulent *Treponema pallidum* these authors carried out the following tests: *Trep. pallidum* complement-fixation test (TPCF), Reiter protein CF test (RPCF), VDRL slide test and *Trep. pallidum* protein cryolysis CF test (TPCP); the antigen for this last test was obtained by eluting spirochaetes from syphilitic rabbits' testicles, differential centrifugation and cryolysis and ammonium sulphate treatment.

Adsorption of syphilitic sera with VDRL, RPCF, TPCF and TPCP antigens was then carried out. Sera adsorbed with VDRL were no longer reactive to VDRL antigen but still reacted with the other 3; on the other hand sera adsorbed with the other antigens still reacted with VDRL antigen. Adsorption of serum with VDRL, RPCF and TPCP antigens did not reduce the titre of TPCF test; adsorption with protein antigen from virulent spirochaetes removed activity with virulent and Reiter protein antigens; adsorption with TPCP antigen did not remove reactivity in VDRL and TPCF tests; sera adsorbed with Reiter's protein and virulent protein were negative in the RPCF test. These facts present evidence that there is an antigen common to virulent and avirulent spirochaetes. When rabbits were injected with RPCF antigen only the RPCF and TPCP tests became positive.

The RPCF test therefore should be specific and of value in tests for syphilis. *T. E. Osmond*

ANDUJAR, J. J. & MAZUREK, Edith E. **The Plasmacrit (PCT) Test on Capillary Blood. Unheated Plasma Screen Test for Syphilis.** *Amer. J. Clin. Path.* 1959, Mar., v. 31, No. 3, 197–204, 1 fig. [14 refs.]

These authors describe a "screen" test for syphilis (PCT) using plasma left over in microhaematocrit capillary tubes; plasma has a higher content of reagin than serum and the use of capillary tubes avoids venepuncture.

The ingredients of the test consist of plasma obtained from heparinized capillary tubes, and VDRL antigen to which is added choline chloride (which avoids the necessity of heating). Into ceramic rings on a glass slide are placed 0·025 ml. of plasma and 0·01 ml. of antigen suspension; the slide is then rotated for 4 minutes and the result read at once. For details the original should be consulted.

2,813 persons were studied by means of 11,480 reagin tests including Kline cardiolipin, Kahn standard, VDRL slide, Kolmer CF and the PCT tests; the respective percentages of positive results were 18·3, 15·0, 23·0, 13·1 and 24·6; thus it will be seen that the PCT was the most sensitive, followed closely by the VDRL. The PCT gave considerably more doubtful results than any of the others; the specificity of the PCT is said to compare favourably with that of Kahn, Kline and VDRL test.

The PCT is quick, inexpensive, causes the minimum of pain and inconvenience and is reproducible; it is stressed that it is only meant to be a screen test and not a diagnostic one. *T. E. Osmond*

GRIFFITHS, S. B., BUCKLE, G. C. & HILL, J. W. **V.D.R.L., Eagle, Price, and Kolmer Tests. A Comparison using 1,029 South African Bantu Sera.** *Brit. J. Venereal Dis.* 1959, Mar., v. 35, No. 1, 40–43, 1 fig.

These authors tested the sera of 1,029 healthy Bantu males by means of these 4 tests in parallel; results are set out in detail in 1 figure and 1 table.

151 (14·7%) sera were positive with 1 or more of the 4 tests; the VDRL was positive in 122, the Eagle in 124, the Price in 75 and the Kolmer in 87; only 57 sera were positive with all 4 tests and 38 were positive with only 1 test. There was considerable disagreement, 20 sera positive with Eagle were negative with VDRL and 18 gave opposite results. Discrepancies were probably not due to technical errors since when any test was positive all 4 were repeated and gave the same results.

It is suggested that diminished sensitivity might be explained by the presence of inhibitory factors in Bantu sera and that decreased specificity was due to non-specific factors; racial and geographic factors may also have affected results. It is concluded that no one of these tests would serve as a screen test and that the incidence of syphilis in the Bantu cannot be estimated accurately by using any or all of these tests.

[What would be of value would be a full clinical examination or, even better, a TPI test of all reactors.] *T. E. Osmond*

ENG, J. **A Note on the Course of Reagin Titres in Chronic Biologic False Positive Reactors.** *Brit. J. Venereal Dis.* 1959, Mar., v. 35, No. 1, 44–6, 1 fig.

11 persons who had positive serum tests for syphilis (STS), negative TPI tests and no evidence of syphilis were investigated by means of quantitative Wassermann (WR) and Meinicke (MKR II) reactions.

With the WR, 1 showed increasing, 6 constant and 1 decreasing titres; 2 were negative and 1 could not be assessed; with the MKR II, 3 showed increasing and 5 constant titres while 3 were negative; 6 patients had received anti-syphilitic treatment.

The clinical diagnoses in 5 cases were: cystopyelonephritis and anaemia, rheumatoid arthritis and possible disseminated lupus erythematosus, circulatory failure and hypertension, psychosis and peptic ulcer.

It is suggested that clinical symptoms and false-positive reactions arise from the same cause and that it is worth while to observe the STS titres in false positive reactors. *T. E. Osmond*

SCHMIDT, H. **Comparison between the Reactivity of Cardiolipin Antigen and a Lecithin-Free Cardiolipin Antigen (Cardchol) in TPI-Reactive and TPI-Non-Reactive Sera.** *Brit. J. Venereal Dis.* 1959, Mar., v. 35, No. 1, 47–52, 1 fig. [32 refs.]

This article is mainly intended to show that there are various antilipoidal antibodies which react with different antigens.

The author tested 177 TPI reactive and 199 TPI non-reactive sera by means of the WR (C-WR-M complement-fixation test [this *Bulletin*, 1956, v. 31, 389] with cardiolipin-lecithin-cholesterol antigen in the proportions of 1 : 5 : 17), Cardchol complement-fixation test with the same antigen but omitting the lecithin, Kahn test with crude antigen, Meinicke test with crude antigen and the TPI test.

Results are set out in 5 tables and 1 figure.

In the TPI-reactive sera ordinary cardiolipin antigen proved superior to Cardchol but in about 50% of the TPI non-reactive sera Cardchol was superior to ordinary cardiolipin antigen. The difference is obviously due to the presence or absence of lecithin; this may be due to syphilitic antilipoidal antibodies having their reaction optimum at a definite level of lecithin whereas these antibodies of other origin have their reaction optimum at a different lecithin level.

It is clear that Cardchol is most reactive when antilipoidal antibodies are non-syphilitic; but Cardchol is more reactive than ordinary cardiolipin antigen in early syphilis before the TPI becomes positive and when the ordinary cardiolipin reactions are still weak. Thus it seems that antibodies against the various constituents of *Treponema pallidum* developed at different stages of syphilis differ from one another. *T. E. Osmond*

CANNEFAX, G. R. **Streptomycin, Sodium Azide, and Merthiolate as Bacteriostatic Agents for Use with the *Treponema pallidum* Immobilization Test.** *Brit. J. Venereal Dis.* 1959, Mar., v. 35, No. 1, 53–4.

Bacterial contamination may render serum specimens unsuitable not only for classical serum tests for syphilis but even more for TPI tests.

A short review of the literature is given and the author reports his own experience.

Streptomycin at a concentration of 100 μgm./ml. did not have any harmful effect on the viability of *Treponema pallidum* [this *Bulletin*, 1955, v. 30, 227] sodium azide in concentrations of 1 : 1,000 to 1 : 8,000 had virtually no effect on TPI titres; Merthiolate [thiomersal] 1 : 1,000 to 1 : 2,000 also had no harmful effect provided there was an adequate concentration of sulphhydryl (as sodium thioglycollate).

T. E. Osmond

ENG, J. **Treponemal Immobilization Test in Expectant Mothers. Results in 142 Reactors to Standard Serological Tests.** *Brit. J. Venereal Dis.* 1959, Mar., v. 35, No. 1, 10–14. [10 refs.]

Sera from 27,445 pregnant women were examined by means of (1) MKR (cardiolipin-lecithin-balsam-of-Tolu antigen), (2) WR (cardiolipin-lecithin-cholesterol antigen), (3) Wadsworth and Brown flocculation test (W-Br with crude beef heart antigen); of these 168 gave positive reactions with one or other test; of these 149 were submitted to the TPI test.

Of 102 women who gave positive MKR or WR reactions 83 (81·37%) were TPI positive and 19 (18·63%) were TPI negative; of 40 who reacted to the W-Br test 3 were TPI positive and 37 TPI negative. In a selected group of 142 women 86 were TPI positive, 80 MKR positive, 80 W-Br positive and 48 WR positive.

Of 142 sera [presumably the same ones] the WR was positive in 55 in 7 of which TPI was negative; the MKR was positive in 97 in 17 of which TPI was negative; W-Br was positive in 131 of which 51 were TPI negative.

When the women were divided into age-groups it was found that in the older ones syphilis was present in 0·692% compared with 0·146% in those born after 1928.

About 70% of the TPI positive women were known beforehand to have syphilis.

It is concluded that the TPI test should be carried out on all who give positive STS without evidence of syphilis and that the W-Br test is over-sensitive.

This article is somewhat difficult to follow but does show that about 20% of positive reactions in antenatal STS testing are non-specific. *T. E. Osmond*

BROWNE, A. S., BISSETT, Marjorie L. & MICHELBACHER, Martha M. **Reproducibility of TPI and TPCF Tests.** *Amer. J. Clin. Path.* 1959, Mar., v. 31, No. 3, 205–12. [24 refs.]

In order to find out how reproducible these tests were these authors tested 2 series of sera (509 in experiment A and 63 in experiment B). The chosen sera were from 3 types of persons: those with positive serum tests for syphilis but without other evidence of the disease, those with clinical evidence of syphilis but negative serum tests, and pregnant women with positive serum tests for syphilis. In experiment A the TPI was positive in 48%, weakly reactive (WR) in 5% and negative in 45%; the corresponding figures for TPCF were 33, 10 and 49; reproducibility was 81% with TPI and 50% with TPCF. The main divergencies were in the weakly reactive sera [as would be expected] and in these the TPI proved better than TPCF. In experiment B the 63 sera were those sent for "routine" treponemal testing; 91% of TPI and 83% of TPCF reproduced exactly the same result when retested on different days.

Complete disagreement occurred in none of the TPI tests and in 15 of the TPCF tests; paired specimens tested in the same batch showed 100% agreement with the TPCF and 97·5% agreement with the TPI.

Detailed results are set out in 8 tables.

It does seem that the TPCF test is not yet very reliable; no doubt improvements in the antigen will eventually make this test more valuable.

T. E. Osmond

LAIRD, S. M. **Elimination of Congenital Syphilis.** *Brit. J. Venereal Dis.* 1959, Mar., v. 35, No. 1, 15–19, 3 figs.

Routine blood testing of expectant mothers can never, alone, eliminate congenital syphilis for a variety of reasons.

In England and Wales the incidence of early acquired syphilis in the female fell from 2,683 in 1931 to 257 in 1956 with the highest peak of 6,970 in 1946; the corresponding figures for the Manchester area were 270 and 4 with a peak of 562 in 1946. No doubt the improvement is due to antenatal blood testing and penicillin treatment. However, the relationship between infectious syphilis in the mother and congenital syphilis in the child has remained virtually unchanged.

While infectious syphilis in the female has almost ceased to be endemic in many parts of Britain especially in the Manchester area [this Bulletin, 1958, v. 33, 119], sporadic cases still appear in many seaports and larger cities. Until these are found early and adequately treated congenital syphilis will not disappear but the elimination of the latter does appear to be in sight.

Statistical details are given in 6 tables and 3 figures.

T. E. Osmond

HOLMES, W. **Gonorrhoea in Ipoh 1958.** *Med. J. Malaya.* 1959, Mar., v. 13, No. 3, 197–200.

During a period of 1 month all medical practitioners were invited to notify cases of gonorrhoea. 123 were obtained including 108 men, 10 women and 5 children. Of 25 hospital cases 23 were acute and 2 chronic; 23 were all infected by prostitutes. Intercourse took place in hotels in 17, in private houses in 6 and elsewhere in 2; introduction was made by taxi-drivers in 11, hotel staff in 3, friends in 3 and not stated 8; places of contact were—bars 16, cabaret 1, streets 2, not stated 6.

The author thinks that supervision of prostitutes would help but that contact tracing would be a better long-term policy [What he means by "the infected prostitute is relatively sterile" is not clear.]

T. E. Osmond

BURGESS, J. A. **Non-Gonococcal Urethritis Contacts.** *Brit. J. Venereal Dis.* 1959, Mar., v. 35, No. 1, 24–6.

250 female contacts of men suffering from non-gonococcal urethritis (NGU) were examined; 159 (63·6%) were referred by husbands and 91 (36·4) by others; 171 were married and 79 were not; ages ranged from 17 to 57 but most fell into the 20–24 age-group. Symptoms included dysuria 3·6%, vaginal discharge 34·4%, "others" 1·2% and none 60·8%; 103 women (41·2%) admitted extra-marital exposure.

In 168 (67·2%) there was cytological evidence of genito-urinary disease and in 82 (32·8%) there was none; 35% showed *Trichomonas* vaginitis and 29·6% endocervicitis or cervical erosions; 32·8% showed nothing abnormal.

The author suggests that these women fell roughly into 3 groups: (1) trichomoniasis, (2) infections of the cervix, (3) non-venereal; this last may include NGU due to causes which were non-infective, *e.g.* certain foods or drugs, contraceptives or trauma.

[It would be interesting to know how many times trichomonads were found in the male partners of women suffering from trichomoniasis.] *T. E. Osmond*

ALBERT, J. & CRONE, R. I. **Keratosis Blennorrhagica (Reiter's Disease?) and its Treatment.** *Arch. Dermat.* 1959, May, v. 79, No. 5, 581–6, 7 figs. [18 refs.]

"The treatment of keratosis blennorrhagica is reviewed, and the difficulties in evaluating the true benefit of therapeutic agents in this disease are discussed.

"Two patients with keratosis blennorrhagica are reported and the management of their illnesses discussed. There was prompt clearing of the first patient's skin lesions when a 10-day course of penicillin and and streptomycin was given during the second month of his illness, but there was little effect on the arthritis. The second patient showed a complete and striking response to prednisolone after other therapy, including corticotropin (ACTH) and various antibiotics, had failed. It is suggested that prednisolone be used in future cases of keratosis blennorrhagica in order to further evaluate its effectiveness.

"No conclusion can be made as to the etiology of keratosis blennorrhagica at present, but its striking similarity to Reiter's syndrome is discussed. It is noted that skin lesions identical to those of keratosis blennorrhagica are being found in increasing numbers of cases of Reiter's syndrome."

KLIENEBERGER-NOBEL, E. **Possible Significance of PPLO in Human Genital Infection.** *Brit. J. Venereal Dis.* 1959, Mar., v. 35, No. 1, 20–23.

Pleuropneumonia-like organisms (PPLO) are known to be pathogenic to cattle and sheep, and are frequently found in human beings.

This author isolated them from 25·5% of 200 males suffering from various conditions as follows: acute non-gonococcal urethritis (NGU) 48%, untreated gonorrhoea 30%, various para-venereal conditions 9·3% and Reiter's disease 10% but none from chronic or cured NGU; 40 boys under 13 were all negative and only 3 out of 100 healthy adults were positive. Cultures were obtained from discharge and scrapings in the test cases and from urine in the controls.

Of women from a VD clinic 56% were positive while in those with genital infections the percentage was 80–90; 20% of obstetric and gynaecological patients were also positive. Complement-fixation tests were positive in 34% of VD patients, 6·1% of medical out-patients, 6·3% of antenatal patients, 20·4% of gynaecological patients, 2·1% of blood donors and 2% of children.

Thus organisms were found and serum tests were positive in a relatively large proportion of VD patients [but this does not prove that PPLO are pathogenic].

T. E. Osmond

CARD, Dorothy H. **PPLO of Human Genital Origin. Serological Classification of Strains and Antibody Distribution in Man.** *Brit. J. Venereal Dis.* 1959, Mar., v. 35, No. 1, 27–34. [22 refs.]

Complement-fixation tests (CFT) were carried out on sera from various sources to detect the presence of antibody to pleuropneumonia-like organisms (PPLO) infection. 2 antigens were employed; both were suspensions of PPLO but one was fresh (F) and the other boiled for 10 minutes in a brine bath at 108°C. (B). For details of preparation of the antigens and technique of the test the original should be consulted.

A total of 56 PPLO strains isolated from the genito-urinary system of humans was examined; antisera were made against pleuropneumonia of cattle, human genital PPLO, human mouth, rat and saprophytic (sewage) PPLO; by this means human genital strains could be distinguished from all the other strains. The following are the percentages of positive results obtained in various persons; VD patients 34·2, medical out-patients 6·1, antenatal patients 6·3, gynaecological patients 20·4, blood donors 2·1 and children under 13, 2·0; in general results were positive roughly twice as often in women as in men (VD patients); the proportion of positive sera in all groups with one or both antigens was F only 43%, B only 21% and F + B 36%. Case histories of 423 VD clinic patients were examined; 18·7% of males and 44·5% of females gave positive CF tests; NGU and VD patients gave similar results, the latter gave more positives than other hospital patients, men with a history of syphilis or yaws gave a high proportion of reactions (PPLO were isolated from 2 of 3 syphilitic chancres) and in 21 patients with Reiter's disease all tests but 1 were negative.

The human genital strains of PPLO fell into 1 serological group and could be distinguished from all the other strains of PPLO; however, in 41 cases the cultural and CF tests showed marked differences.

This article should be studied in connexion with that by KLIENEBERGER-NOBEL [above]. *T. E. Osmond*

HARRISON, L. W. **Diagnosis of Trichomonad Infestation by Examination of Stained Films.** *Brit. J. Venereal Dis.* 1959, Mar., v. 35, No. 1, 38–9, 1 fig.

The diagnosis of *Trichomonas vaginalis* (TV) is usually made by identifying the living organism by means of dark ground or simple axial microscopy.

This author, however, recommends straining a fixed film which has the advantages that it can be examined at leisure and that one is not dependent on the waving of flagella. The stain should be Loeffler's alkaline methylene blue which has become polychrome with age; the film is fixed by heat and covered with the stain for 45 minutes, mopped and allowed to dry; it appears to be better than Leishman or Giemsa stains.

The distinguishing features are axostile, undulant membrane and flagella, but diagnosis does not depend on seeing *all* these features; in the photomicrograph [which cannot be reproduced in an abstract] the distinguishing features are definite outline, granular cytoplasm and the oval or pear-shaped nucleus stained less intensely than the nuclei of other cells; the axostile can also sometimes be seen.

[The abstractor very rarely (dares to) disagree with Colonel Harrison but surely one usually wants an immediate diagnosis, as with a syphilitic chancre, and except in the case of the skilled microscopist waving flagella are easier to spot than the features described above; incidentally should the word not be spelt axostyle?] *T. E. Osmond*

WILLCOX, R. R. **Treatment of Vaginal Trichomoniasis with Gyno-Sterosan.** *Brit. J. Venereal Dis.* 1959, Mar., v. 35, No. 1, 35–7. [43 refs.]

A review of the literature shows that a very large number of remedies have been tried in the treatment of this condition but that none have had much success.

49 patients (41 white and 8 Negresses) were treated intra-vaginally with 2 tablets of Gyno-sterosan (5 : 7 dichloro-8-hydroxy-quinaldine) each night for periods up to 3 weeks; 15 patients gave no history of venereal disease but the remainder appear to have been promiscuous [which may account for some of the failures]. 43 were followed up for various periods up to 3 months; results were satisfactory in 23 (53·5%) and in 17 *Trichomonas* were found later.

No side effects were noted and it is stated that Gyno-sterosan is effective against vaginal thrush.

[Unfortunately it is not known how regular the treatment was nor how many of the failures were due to reinfection; unless these 2 factors can be assessed it is impossible to estimate the efficacy of any given form of treatment.] *T. E. Osmond*

OTHER COMMUNICABLE DISEASES

The order of papers in this Section is as follows: Tetanus; other diseases

MATVEYEV, M. P. & PAUL, S. S. **Study of Tetanus Cases (at the Kalavati Saran Children's Hospital in 1956–58).** *Indian J. Child Health.* 1959, Apr., v. 8, No. 4, 181–94.

This is a survey of patients with tetanus studied at the Kalavati Saran Children's Hospital, Delhi, between April 1956 and October 1958: 47 children were admitted, 28 in the neonatal period. The high incidence in the neonatal period is explained by the primitive hygiene of home deliveries: 34 of the 47 children died and 4 other children were taken home in a moribund condition. Treatment consisted of anti-tetanic serum and sedation by barbiturates and chlorpromazine: delta-cortril was given to a few patients but no definite claims are made as to its effectiveness.

A. B. Christie

ADAMS, E. B., WRIGHT, R., BERMAN, E. & LAURENCE, D. R. **Treatment of Tetanus with Chlorpromazine and Barbiturates.** *Lancet.* 1959, Apr. 11, 755–7.

In a comparison of chlorpromazine with a combination of chlorpromazine and phenobarbitone in the treatment of tetanus in a non-neonatal group [56 patients], no significant difference in effect was found. In a neonatal group [40 patients] there was no significant difference in effect between chlorpromazine and a combination of barbiturate and chloral. Chlorpromazine is, however, a useful drug in achieving relaxation of spasm and combination with a barbiturate avoids excessive dosage with either. There is a maximum dose of chlorpromazine above which antitetanic activity is not increased and may in fact be diminished: for non-neonates the critical dose is probably 200–300 mgm. If the drug is given more frequently than every 2 hours there may be diminishing response to succeeding doses: this may be avoided by alternating chlorpromazine with a barbiturate. Acetylpromazine, shown experimentally to have 10 times the effect of chlorpromazine against tetanus, did not appear to have any advantage clinically.

[For a previous study, see this *Bulletin*, 1958, v. 33, 746.] *A. B. Christie*

DWYER, B. & LAZARUS, L. **The Treatment of Severe Tetanus.** *Med. J. Australia.* 1957, Aug. 17, v. 2, No. 7, 249–50.

This article records in detail the successful treatment of severe tetanus in a man aged 42. Tubocurarine was used as the muscle relaxant, ventilation with air was carried out *via* a tracheostome by an Aga pulmospirator, and soluble phenobarbitone was used for sedation. *A. B. Christie*

REGAMEY, R. H. L'immunisation active contre le tétanos. [**Active Immunization against Tetanus**] *Ergebn. Mikrobiol. Immunitätsf.* 1959, v. 32, 270–381, 12 diagrams. [Numerous refs.]

This is a long review article by an experienced worker in the field of tetanus prophylaxis; it is well documented and there are approximately 1,000 references which are quoted in full. The method of dividing the article up into sections covering Introduction, Tetanus Toxin, Tetanus Toxoid, Production of Basal Immunity, Secondary Response and so on has much to recommend it, but it leads to a considerable amount of repetition and does not always make for smooth reading. On the other hand the table of contents helps the reader who wants to turn back, and the very accurate author and subject reference index, an outstanding feature of this journal, is of the greatest help with an article of this type.

Although most of the attention is devoted to work connected with active immunization against tetanus some consideration is given to the history of immunization of animals with toxin or modified toxin for the preparation of antitoxin for passive protection or therapy, and it is difficult to understand why no mention is made of the pioneer work of KITASATO or BEHRING. With regard to the history of the detoxifying action of formaldehyde on tetanus toxin the author is fair to LÖWENSTEIN and DESCOMBEY in opening the field to RAMON. From then onwards a comprehensive story is developed and almost every facet of active immunization against tetanus receives due consideration, and the assessment of the various procedures is reasonable. The author obviously favours the subcutaneous or intramuscular route of injection for the particular agent used and, although he is well aware of the highly potent toxoid preparations now available by employing the casein hydrolysate medium of Mueller and Miller, and the satisfactory antibody response after intradermal inoculation, he feels that the various difficulties associated with intradermal inoculations make it unsuitable for mass immunization. [In this connexion it is of interest to recall [BARR, SAYERS & STAMM, this *Bulletin*, 1959, v. 34, 741] that the British Army for the Home Commands is now employing the intradermal method for the immunization of troops against the enteric group of fevers and tetanus with a combined prophylactic. The immunization programmes set out in the article under review for the Armed Forces of Great Britain, France, Switzerland and United States are all dated, but with rapidly changing procedures their value seems to be doubtful.] *H. J. Bensted*

CHIANG CHUNG-CHOU. **Efficacy of Simultaneous Immunization with Live Brucella Vaccine and Tetanus Toxoid.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, No. 10, 1629–33. [Translated from Russian.]

"(1) When guinea-pigs were subjected to the simultaneous action of live 19-BA brucella vaccine and tetanus toxoid the immune response in relation to brucellosis was the same as in animals immunized solely with brucella vaccine, *i.e.*, tetanus toxoid acting simultaneously with brucella vaccine did not affect the course of the development or the decline of the immune response to brucellosis. The tetanus antitoxin titres of the sera of the animals immunized with the 2 antigens simultaneously were considerably higher than in the animals immunized with tetanus toxoid alone.

"(2) Guinea-pigs were uniformly resistant to a virulent strain of *Br. melitensis.* and tetanus toxin after simultaneous immunization by injection of both antigens and when they were used separately.

"(3) Subcutaneous inoculation with live 19-BA brucella vaccine may be used with success in combination with active immunization against tetanus."

PAUL, J. R. & MCCLURE, W. W. **Epidemic Hemorrhagic Fever Attack Rates among United Nations Troops during the Korean War.** *Amer. J. Hyg.* 1958, Sept., v. 68, No. 2, 126–39, 7 figs. [10 refs.]

A comparison was made between the attack rates among non-Korean troops stationed at 13 arbitrary points scattered across the combat zone in Korea in the spring and summer of 1952 and the spring of 1953. The denominators for these rates were estimates of

the man-days of exposure of divisions stationed at the points, and the numerators were 705 confirmed cases admitted in these periods to the specially designated haemorrhagic fever hospital. The rates for the different positions varied from 3·2 to 27·9 per million man-days, being highest in the centre of the line of combat, rather less to the west and considerably less on the east. This central and western area had previously been cultivated intensively, but with the displacement of all the indigenous population for 2 years it had become profusely overgrown with underbush and weeds and the fauna had altered correspondingly. To the east the zone was much more mountainous and wooded and had not suffered the same change.

In the spring of 1953 61 patients suffering from haemorrhagic fever and 61 controls selected from another hospital were interviewed to determine what they had been doing and where they had been during a period of a month before the onset of illness. A higher proportion of the haemorrhagic fever patients than of the controls, 95% compared with 72%, came from the forward areas above the "farm line", *i.e.* from the abandoned farm land. Attack rates 50 miles or more to the south were much lower than in the combat zone. *J. Knowelden*

REID, J. D. **Cat Scratch Disease.** *New Zealand Med. J.* 1959, Feb., v. 58, No. 323, 39–44, 4 figs. on 2 pls. [14 refs.]

In this paper the author reports the results of the cat scratch disease skin test in 116 patients who had been referred for this investigation. Included among these were the 38 patients who were described in a previous report [this *Bulletin*, 1957, v. 32, 324]. The antigen used in the first series was derived from a macerated lymph node but in addition to this a second antigen obtained from pus of a cervical abscess has been employed.

The 116 patients referred for testing were suffering from types of illness classed as regional lymphadenitis following cat scratch or without any skin abrasion, generalized lymphadenopathy, abdominal pains (?), mesenteric adenitis and miscellaneous illnesses. There were 40 positive skin test results distributed among all the types of illness—*e.g.* 11 positives in 20 cases of lymphadenitis following cat scratch, 10 positives in 27 cases of lymphadenitis with no skin abrasion and 5 positives in 14 cases of generalized lymphadenopathy. These results which were not uniform in the 2 tests with the 2 different antigens are discussed. "The validity and specificity of these tests . . . have been examined on clinical grounds and by correlation with results of complement fixation tests at surgical biopsies."

The clinical manifestations of the disease are described and recent published work is noted.
M. E. Delafield

LAIDLAW, A. J. **An Epidemic of Unknown Aetiology.** *Lancet.* 1959, May 30, 1141–2.

This is an account of an epidemic of undiscovered aetiology which occurred in general practice in Worcester in March-April, 1957 and in which 48 persons were taken ill. A conspicuous feature in all the patients was the sudden onset of symptoms of which intermittent frontal headache was the most frequent. Other common symptoms were nausea, giddiness, sore eyes, vomiting and sore throat. The signs found on examination were bilateral conjunctivitis (14 cases), fever of 99°F. to 101°F. (13), slight neck rigidity (8) and injected fauces (6). Cases of the disease occurred in all age-groups from 0–10 years to 71 + years and the distribution was about equal in the sexes. The duration of the illness was usually 1 or 2 days and complete recovery followed within 7 days.

Virus studies of specimens from 28 patients (16 samples of faeces, 8 throat swabs, 10 of blood taken within 3 days of onset of the illness and 19 of convalescent blood) gave negative results.

Reference is made to the College of General Practitioners Research Newsletter No. 15, 1957, which records that "General practitioners were notified of the outbreak and positive returns were received from Worcester, Malvern, Coventry, and Callington (Cornwall). The College of General Practitioners named this symptom-complex L.W.57." *M. E. Delafield*

ZOONOSES

In this section the abstracts are arranged as far as possible in the following order: General; Anthrax; Brucellosis; Tularaemia; Leptospirosis; Ornithosis; others.

For such tropical diseases as Trypanosomiasis, Leishmaniasis, Rickettsial Fevers, Yellow Fever, Plague, etc., see TROPICAL DISEASES BULLETIN.

THIENPONT, D., WIKTOR, T. J., MORTELMANS, J., VANDENABBEELE, K. G., BICHE, Y., FAGARD, P. & PINCKERS, F. Recherches sur la brucellose bovine et humaine au Congo Belge et au Ruanda-Urundi, à propos d'une enquête dans le territoire d'Astrida (R-U). [**Bovine and Human Brucellosis in the Belgian Congo; an Investigation in Astrida, Ruanda-Urundi**] *Ann. Soc. Belge de Méd. Trop.* 1958, Dec. 31, v. 38, No. 6, 1049–73, 1 map & 2 figs. on pl. [17 refs.]

The authors review the scanty reports of brucellosis in the Belgian Congo and Ruanda-Urundi. Indigenous cases so far have only yielded *Brucella abortus* with the exception of 2 Africans who in 1952 had come from Ituri and who yielded *Br. melitensis.* There are also records in Astrida of 3 Europeans being found in 1951–2 to be infected with *Br. melitensis.* The strains of *Br. abortus* isolated by the authors from 67 cattle and 1 woman all conformed to the type described by BEVAN (*Brit. Med. J.*, 1930, v. 2, 267) in not requiring a reduced oxygen tension for growth, being little inhibited by thionine but being agglutinated by a monospecific *Br. abortus* serum. The investigation in cattle carried out by the authors in Astrida (Ruanda-Urundi)

showed a remarkable number of beasts (5·03%) to exhibit hygromas, *i.e.* collections of fluid lying subcutaneously or between tissue planes and not necessarily connected with joints. Usually only 1 hygroma was present in an infected animal but 2 or more were occasionally found; one beast exhibited 11. By agglutination tests 6·76% of the cattle examined appeared to be infected with brucellosis. 63 of the 67 successful cultures of *Br. abortus* from cattle were obtained from puncture of hygromas.

In a survey of human brucellosis among owners of infected cattle, the authors found a greater number to show skin sensitivity than sero-agglutinins. A positive blood culture was obtained from one woman who, beyond mild recurrent fever, gave no history particularly suggestive of brucellosis. 2 of the staff employed in the investigation developed brucellosis confirmed by rising titres for sero-agglutinins.

[The authors do not state if evidence of brucellosis in sheep, goats or pigs, in Astrida was sought although the estimated numbers of these animals in that district are given.] *Frederick J. Wright*

KNOTHE, H., ZIMMERMANN, O. & HAVEMEISTER, G. Über die Tularämie in Schleswig-Holstein. Ein epidemiologischer Bericht anlässlich des Wiederauftretens der Tularämie in Eiderstedt im Winter 1957/1958. [**Tularaemia in Schleswig-Holstein**] *Deut. Med. Woch.* 1959, May 8, v. 84, No. 19, 906–9, 932, 1 fig.

Since 1948 a total of 428 cases of tularaemia have been reported in Germany. Tables set out the yearly incidence which was very variable. Endemic areas are the northern provinces of Mecklenburg (160 cases occurred in Peenemündung during 1948–57 and 93 cases in Main-Franken during 1950–7) and Schleswig-Holstein (138 cases in the Eiderstedt peninsula in 1951–8). The number of cases occurring elsewhere in Germany was very small. Much of this paper is devoted to discussion of the experience in Eiderstedt where tularaemia first appeared in the winter of 1950–1. It is possible but uncertain that the infection was introduced by hares imported from Yugoslavia for hunting or by birds from Scandinavia since in Sweden in 1950 an increase in the disease had been observed. In Eiderstedt almost all persons who acquired the infection were proved to have had contact with hares. The infection in different rodents is described and the meteorological conditions which might foster the infection are also considered. A map illustrates the distribution and mode of infection in the cases—about 30 in number—which occurred in 1957–8 in Eiderstedt. *M. E. Delafield*

FUKADA, M. & OHARA, S. **Epidemiological Studies on the Tularemia in Japan.** *Fukushima J. Med. Sci.* 1957, Sept., v. 4, No. 3, 147–54, 2 figs. [30 refs.]

The authors record that between 1924 and 1955 there were 717 reported cases of tularaemia in Japan and it is known that there were many other patients treated for tularaemia. The distribution of the cases according to the prefectures, age, sex and occupation are recorded. The usual source of infection in Japan is the rabbit and the incidence was greatest in farmers. In most cases infection occurred by contagion during manipulation of wild rabbits either alive or dead. In a few cases handling of pheasant, chicken, cat or squirrel was responsible and the authors note that recently the disease was acquired from a Japanese black bear. In only 3 cases was the infection transmitted by the bite of a tick. There were 24 recorded cases of laboratory infection and H. OHARA, showed in 1944 that heart blood of a dead rabbit could cause infection through unbroken human skin. The ulcero-glandular and glandular forms of the disease were the most frequent, it being more frequent to find regional lymph node enlargement with no recognizable primary skin lesion than with a primary lesion. This differs from the experience in U.S.A. [FOSHAY, this *Bulletin*, 1941, v. 16, 26]. Occulo-glandular, typhoidal, rhinoglandular and tonsilloglandular forms were all uncommon. No fatal case has been reported in Japan. When the inguinal glands are affected there is a clinical resemblance to lymphogranuloma venereum and the histology is also similar. *Frederick J. Wright*

SASE, W. **Epidemiological Studies on *Yato-byo* (Tularemia in Japan) with the Aid of the Skin Test. II. A Survey in Bandai Highland in 1957.** *Fukushima J. Med. Sci.* 1957, Dec., v. 4, No. 4, 179–90, 2 figs. [15 refs.] **III. The Criteria of the Skin Test.** *Ibid.*, 205–15, 1 fig. [15 refs.]

The author has previously described the results of skin tests for tularaemia carried out in 1956 during a survey on 5,327 people living in the Bandai Highland [this *Bulletin*, 1958, v. 33, 1043]. He now reports on a repetition of the survey made in 1957. In the interval the housewife of a family of 6, all of whom were negative when tested in 1956, acquired tularaemia by skinning and preparing for food a killed wild rabbit. After an incubation period of 4 days the patient became feverish and 2 days later exhibited a painful axillary lymphatic gland. She responded well to streptomycin and chloramphenicol. The skin tested on the 6th day after infection showed both erythema and thickening. Sero-agglutinins appeared between 2 to 4 weeks after infection, were maximal at 1 : 640 at 4 weeks and persisted at 1 : 160 for at least 1 year at which time the skin test showed an increased reaction. The family all exhibited erythema of 10 × 10 mm. without thickening on skin-testing at the beginning of the mother's illness but no erythema or thickening when retested a year later and at no time were sero-agglutinins present.

Statistical analyses of the skin tests carried out in 1957 compared with those of 1956 suggested that only areas of erythema greater than 14 mm. in diameter were to be interpreted as positive and that increase in thickening to over 2 mm. gives good correlation with this degree of erythema. Rather more than one-half of the population tested showed positive reactions and there appeared to be an increased chance of infection having occurred with increasing age.

[See also LJUNG, this *Bulletin*, 1958, v. 33, 1132 and 1959, v. 34, 628.] *Frederick J. Wright*

MITROFANOVA-PERFIL'EVA, E. B. **The Significance of Food Products in the Epidemiology of the Leptospiroses.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1957, v. 28, Nos. 9/10, 1272–6. [Translated from Russian.]

Cases of leptospirosis probably due to the ingestion or handling of contaminated foodstuffs are reported not infrequently, so the author carried out experiments to determine the time of survival of leptospires in different types of liquid, semi-liquid and solid foods. 0·5 ml. aliquots of a virulent culture of *Leptospira icterohaemorrhagiae* were added to 5 ml. quantities of the first 2 varieties and the same volumes were dropped on to the surface of 1·0 gm. amounts of the solids. Survival of the leptospires was determined by microscopical examination of samples of the foods taken at intervals until no living organisms were seen. In parallel tests the infected foods were held at 16–20°C. and 4–5°C. during the period of observation.

The results are set out in the table and show that survival times are shortest in sour milk and cranberry jelly, which are acid in reaction, and relatively short in meat and meat products. In most instances the leptospires survived longer at the lower temperature.

Maximum Periods of Retention of Viability of Pathogenic Leptospires in Foods.

Type of food products		Food product	Maximum period of retention of viability	
			At 16–20°	At 4–5°
Liquid	1	Potato soup	11 days	13 days
	2	Sunflower oil	8 hr.	2 days
	3	Milk	24 hr.	2 days
	4	Sour milk	Less than 10 min.	Less than 10 min.
Semi-liquid	5	Wheat gruel	4 days	5 days
	6	Fish in jelly	24 hr.	2 days
	7	Jellied beef	24 hr.	2 days
	8	Cranberry jelly	Less than 10 min.	Less than 10 min.
Solid	9	Cooked potatoes	24 hr.	2 days
	10	Butter	6 hr.	8 hr.
	11	Cooked meat	2 hr.	4 hr.
	12	Raw meat	30 min.	2 hr.
	13	Sausages (small)	30 min.	30 min.
	14	Black bread	30 min.	30 min.
	15	White bread (86% long loaf)	1 hr.	1 hr.

In another series of experiments the virulence of *L. icterohaemorrhagiae* was tested after 24 hours in potato soup, wheat gruel and milk which were 3 of the most favourable media. Young guineapigs and white mice were infected with the food either by inoculation or by mouth and were kept under observation. Temperatures were recorded daily and, if a rise occurred, cultures were made from heart blood. Animals which died were autopsied and the tissues examined microscopically for the presence of leptospires. All survivors were killed during the 4th week, examined in the same way and, in addition, serum was tested for the presence of agglutinins. Of the 14 guineapigs given the various foodstuffs 3 died and 8 others showed other evidence of infection. Among the 25 mice similarly treated there was 1 death and 12 others with evidence of infection. Of 25 control mice infected by the same routes with a virulent culture 2 died and 13 had signs of infection. [No control guineapigs were used.]

There is therefore experimental evidence that leptospirosis can be contracted by the ingestion of contaminated foodstuffs. *J. C. Broom*

PEREDERI, S., MĂGUREANU, E., SEFER, M., ISRAEL, H. & BERCEA, I. Leptospirozele în regiunea Constanța. (Studiu epidemiologic si de laborator.) [**Leptospiroses in the Region of Constantza**] *Microbiol. Parazitol. Epidemiol.* Bucharest. 1959, Mar.–Apr., v. 4, No. 2, 123–30, 2 figs. [12 refs.]

The English summary appended to the paper is as follows:—

"Epidemiologic data and laboratory investigations concerning an epidemic of leptospirosis in the region of Constantza which included 159 cases, are discussed.

"The epidemic occurred during the summer months (July-August) and involved agricultural workers and children.

"The disease was generated by the existence of leptospirosis in domestic animals, and especially in pigs. Water was the main route of transmission and this lent the epidemic its hydric character. The epidemiologic situation in the region of Constantza requires continued investigations in order to detect the natural sources of leptospirae and to take organizational steps on a regional scale, with the cooperation of sanitary and sanitary-veterinary bodies."

MURASCHI, Thelma F., with the technical assistance of Marjorie HULETT & Anne LEONE. **Latex-Leptospiral Agglutination Test.** *Proc. Soc. Exper. Biol. & Med.* 1958, Oct., v. 99, No. 1, 235–8.

An antigenic suspension for use in a macroscopic agglutination test for routine diagnostic work was prepared as follows: a heavy suspension of leptospires, killed with 0·5% formalin, washed and resuspended in 0·5% formalin in normal saline, was mixed with a suspension of polystyrene latex particles. The optimum proportions of the 2 constituents were determined by titrating various mixtures against positive antisera. [The original should be consulted for details of the preparation and standardization of the suspensions.]

In carrying out the test, equal volumes (1·0 ml.) of serum and antigen were mixed in 12 × 75 mm. tubes; the tubes were corked and incubated for 90 minutes at 56°C. After incubation the tubes were centrifuged at low speed and then examined by transmitted light against a dark background. The aggregates were kept suspended by tapping the tubes with the fingers during the examination.

For use in a qualitative screening test, a pool was made containing equal volumes of suspensions of *Leptospira icterohaemorrhagiae*, *L. pomona* and *L. canicola* which are the 3 serotypes most commonly encountered in the author's diagnostic work. The pooled suspension was found to give a high degree of cross-agglutination with antisera prepared against 17 different serotypes of leptospires.

In a series of tests with single antigens, sera from

human cases of leptospirosis generally showed higher titres with latex suspensions than in the standard agglutination-lysis test. They all also reacted positively in a dilution of 1/100 (the only dilution used) with the pooled suspension when the infection was caused by one of the 3 serotypes present in the pool. Sera from cases infected with other serotypes generally, but not invariably, reacted positively with the pooled suspension.

The latex suspensions remain stable for at least 2 years, and the author considers that they offer a useful alternative to living cultures for diagnostic work.

J. C. Broom

MEYER, K. F. **Some General Remarks and New Observations on Psittacosis and Ornithosis.** *Bull. World Health Organization.* Geneva. 1959, v. 20, No. 1, 101–19. [Numerous refs.]

This paper reviews and brings up to date our knowledge of the ecology of psittacosis-ornithosis viruses. Prominence is given to the increasing importance of infection in poultry—turkey, duck, domestic fowl and pigeon—both from the public health and economic point of view. Natural infection has now been found in 98 species of birds belonging to 9 orders. Increasing numbers of mammalian species, other than man, acting as host to these viruses are being found, but they continue to be relatively unimportant as a source of human disease. Serological evidence is suggesting that infection of man, often mild or inapparent, is much more widespread than had been thought. And the absence of evidence of an avian source of much of this infection suggests that it is man-to-man transmission of strains that have become adapted to man.

S. P. Bedson

Diseases due to Fungi

For papers on systematic mycology, see the section in Bacteriology, below. Papers on Blastomycosis (South American type), Coccidioidomycosis, Mycetoma and Rhinosporidiosis are abstracted in the TROPICAL DISEASES BULLETIN

RIDDELL, R. W. [M.D., F.R.C.P.] & STEWART, G. T. [B.Sc., M.D., D.T.M. & H.] [Edited by.] **Fungous Diseases and their Treatment.** pp. xvii + 256 + 8, 145 figs. 1958. London: Butterworth & Co. (Publishers) Ltd., 88, Kingsway, W.C.2. [45s.]

The 31 papers which go to make up this book were read at a Symposium on Fungous Diseases held under the aegis of the British Postgraduate Medical Federation at the Institute for Diseases of the Chest, Brompton Hospital, in July 1957. Financial support for the symposium was given by Messrs. E. R. Squibb and Sons.

It is not in any way a textbook and only in part will it be used for reference but it does bring together the experiences of workers, mostly from the United Kingdom, the U.S.A. and France, who are actively engaged in the study of various aspects of fungous disease.

The book is divided into 2 parts. Part 1 covers pathology, clinical features and epidemiology while Part 2 deals with treatment.

Part 1 contains 22 articles each by a different author and the diversity of subjects is matched only by the variation in the standard of work presented. All the papers are short—no doubt because of the limited time allowed for presentation—and most are liberally illustrated by plates of excellent quality. A straightforward essay by R. W. RIDDELL entitled *The Role of Fungi as Human Pathogens* (pp. 3–24) which surveys briefly most of the field of medical mycology, is followed by interesting observations on the various histopathological pictures seen in fungal infections in Britain by W. St. C. SYMMERS (pp. 25–49). Next come 5 short papers on various aspects of tinea infections, followed by 7 papers on moniliasis. Of these a short report by T. ANDERSON (pp. 84–87) on the increased incidence of positive cultures of *Candida albicans* in the sputum of patients suffering from respiratory disease after antibiotic therapy was of interest. Of "1,000 patients receiving broad spectrum antibiotics studied mycologically, no example of serious effects attributable to *C. albicans*" was detected.

F. MARIAT (pp. 114–22) of Paris gives a condensed survey of infections due to aerobic actinomycetes with interesting tables showing the characteristics of the grains and cultures of the more important species and this paper is followed by 3 on aspergillosis. C. J. FULLER contributes a note on *Farmer's Lung* (pp. 138–41) and then comes a longer detailed account of the *Serological Diagnosis and Epidemiological Aspects of Histoplasmosis* (pp. 142–57) by Charlotte C. CAMPBELL in a paper with 45 references. *Histoplasmin Testing* (pp. 158–69) in different areas is similarly treated by Phyllis Q. EDWARDS.

Part 1 ends with a concise and valuable account of the *Radiology of Pulmonary Mycoses* (pp. 170–79) by J. W. PIERCE. The standard of the reproductions of radiographs in this section is excellent.

Part 2 contains 9 papers dealing with the treatment of fungous infections. *The Mode of Action of Antifungal Drugs* (pp. 183–91) is discussed briefly by Gordon T. STEWART and this is followed by a more detailed consideration by E. DROUHET (pp. 192–207) of the therapeutic use of these drugs, with particular emphasis on nystatin. This paper, which is illustrated with abundant tables of comparative data, lists 64 references.

The *Treatment of Fungous Infections of the Skin*

(pp. 208–12) is considered in its theoretical aspects by A. J. E. Barlow in a particularly useful paper, while Brian Russell (pp. 213–16) gives a short account of some practical applications and J. M. Beare (pp. 217–20) considers ringworm in children. R. F. Jennison (pp. 221–25) contributes his experience on nystatin which he found more valuable than gentian violet or amphotericin B in the treatment of vaginal moniliasis and O. S. Tubbs (pp. 226–33) records the results of the treatment of 23 patients with actinomycosis seen at the Thoracic Unit of St. Bartholomew's Hospital, emphasizing the fact that with adequate penicillin therapy, surgery rarely has any part to play. N. S. Plummer discusses the *Treatment of Aspergillosis* (pp. 234–40) which he divides into 3 main types: (a) allergic, (b) saprophytic, and (c) septicaemic and, finally, M. L. Furcolow (pp. 241–56) describes encouraging preliminary results of the treatment of histoplasmosis and cryptococcosis with amphotericin B.

For those interested in fungous diseases and who would have liked to have attended this symposium, this book will prove a useful substitute and a valuable record. It is a pity in many cases that the papers are so short; no doubt they were amplified by discussion at the time of the meetings, but in spite of this there is a great deal of information covering a wide field condensed into these 31 papers and 256 pages, and the many references add to the value of the whole.

The book is well printed on glossy paper and the numerous illustrations are of a high standard.

Peter Abbott

Kirk, R. **Mycoses of Malaya and Singapore.** *J. Trop. Med. & Hyg.* 1959, v. 62, No. 1, 10–17. [30 refs.]

The superficial mycoses are among the most common of minor diseases in Malaya whereas the systemic fungous diseases are rare. This account is in large measure an "annotated bibliography" of mycotic disease seen at Singapore and, as well as recording geographical distribution, it gives clinical information about many of the conditions. It forms a most useful summary of local knowledge of fungous infection and should be read in the original by those interested in this subject and its importance in the Far East.

Peter Abbott

Marples, Mary J. & Bailey, Margaret J. **A Search for the Presence of Pathogenic Bacteria and Fungi in the Interdigital Spaces of the Foot.** Reprinted from *Brit. J. Dermat.* 1957, Nov., v. 69, No. 11, 379–88. [12 refs.]

A survey was made of the pathogenic bacteria and fungi in the fourth interdigital space of the foot of 175 subjects, mostly students at the University of Otago, New Zealand. 45 showed no abnormality of the space, 96 had asymptomatic maceration or scaling and in 34 the space was abnormal and subjective symptoms were present. Fungus was found in 8·9% of the normal feet, 12·5% of those with an asymptomatic abnormal space and in 58·8% of those with symptoms.

Coagulase positive staphylococci were found in 8·9% of the normal interspaces, in 9·4% of abnormal asymptomatic interspaces and in no less than 64·7% of those with symptoms; a statistically significant observation. In addition, the recovery of both a pathogenic fungus and a pathogenic staphylococcus from those with symptoms occurred in 47% as opposed to less than 4% in the other 2 groups; a finding which is also statistically significant. This association is discussed.

Peter Abbott

Marples, M. J. **Some Problems in the Ecology of the Dermatophytes.** *New Zealand Med. J.* 1959, Feb., v. 58, No. 323, 64–9. [14 refs.]

This paper is concerned with the distribution, epidemiology and transmission of the dermatophytes seen in New Zealand. *Microsporon canis* is the predominant cause of scalp and body ringworm, the source of infection usually being the kitten. *M. audouini* is rare and *M. gypseum* uncommon. Trichophyton species, particularly *Trichophyton mentagrophytes*, have been most frequently isolated from cases of tinea pedis. *T. rubrum* appears to be increasing especially in the North Island, while *T. verrucosum* is most commonly isolated from human ringworm contracted from cattle.

Peter Abbott

Herpay, Z. & Mészáros, K. Egy trichophytia járvány tanulságai. **[An Outbreak of Trichophytosis]** *Népegészségügy.* Budapest. 1958, Aug.–Sept., v. 39, Nos. 8/9, 205–7, 1 fig.

An account is given of an outbreak of trichophytosis which occurred in 1956 in a Hungarian village of 1,800 inhabitants. The first cases occurred in November in parts of the village which were widely separated from each other; 34 cases were observed among 820 persons investigated. Children aged up to 10 years were mainly affected (16 cases) and the lesions were most frequently observed on the scalp and forearms. A possible connexion with infected animals could only be established in 12 instances, and the infection was thought to have been derived from decaying plant material, probably straw or maize stalks.

D. J. Bauer

Raubitschek, F. **Infectivity and Family Incidence of Black-Dot Tinea capitis.** *Arch. Dermat.* 1959, Apr., v. 79, No. 4, 477–9.

In an epidemiological survey at the Hadassah University Hospital of 150 families comprising 952 members of whom 602 were below the age of 14 years, the author estimated the overall incidence of tinea capitis due to *Trichophyton violaceum* at 46·6%. The incidence in families where there was no adult carrier was 42·6% with a slightly higher incidence amongst boys; whereas, in families where an adult carrier (almost exclusively female) was present, the incidence reached 60·6%. This higher incidence suggests, according to the author, that the home might be even more important than the school as a source of infection. The decline in the number of infections in individuals above the age of 8–9 years and its virtual absence in

adult males is attributed by the author to the influence of sex hormones. All the patients in this investigation were members of immigrant families from North Africa and from Middle East countries where the incidence of this disease is high.

C. J. La Touche

BLANK, H. & ROTH, F. J., Jr., with the assistance of W. W. BRUCE, M. F. ENGEL, J. G. SMITH, Jr. & N. ZAIAS. **The Treatment of Dermatomycoses with orally administered Griseofulvin.** *Arch. Dermat.* 1959, Mar., v. 79, No. 3, 259–66, 6 figs. [16 refs.]

Griseofulvin is a colourless neutral thermostable antibiotic isolated from *Penicillium griseofulvin.* After the successful use of this antibiotic in a case of widespread cutaneous *Trichophyton rubrum* granulomas 31 patients with various mycotic infections were treated. The daily dose of 1 gm. seemed to be adequate although the minimum effective dose and the optimum dose have not yet been established for all types of infection. Tinea corporis usually cleared in 1 to 2 weeks, itching ceasing in 3 to 5 days. Tinea pedis improved in 1 to 2 weeks but sometimes required 3 or 4 weeks to clear completely. Tinea capitis improved in 2 or 3 weeks but sometimes required more prolonged treatment. Onychomycosis required 3 or 4 months to clear; before the normal nail growth was seen gradually replacing the distal diseased portion. The optimum duration of therapy for onychomycosis is not yet known with certainty. Cultures of epithelial lesions usually became negative in 1 week although direct examinations were often positive for a week or two longer than this, while infected nails and hair appeared to contain viable fungi until the involved portions were replaced by healthy new growth.

Toxic reactions appeared to be minimal in therapeutic doses. One patient, however, developed an urticaria-like drug rash after 6 weeks' continuous therapy and other patients complained of mild gastro-intestinal stress and headache.

It is too early to state whether recurrence of infection is likely to occur.

Infections caused by *Candida albicans, Malassezia furfur* and *Blastomyces dermatitidis* did not appear to respond to this therapy. *H. T. H. Wilson*

SEABURY, J. H. & DASCOMB, H. E. **Experience with Amphotericin B for the Treatment of Systemic Mycoses.** *Arch. Intern. Med.* 1958, Dec., v. 102, No. 6, 960–76, 1 fig.

This paper deals with the use of amphotericin B in combating systemic mycoses in various preparations and by various routes. The authors find that a new preparation in which the substance is combined with sodium deoxycholate buffered with sodium phosphate gives rise to less toxic effects and is more effective than previous preparations. They recommend the intravenous route and local instillation with dosages of 1·3 to 0·25 mgm. per kgm. of body weight, and 30 mgm. respectively. Intrathecal injection is also advocated. The method of use in this case is to remove some spinal fluid, inject 20 mgm. of sodium succinate ester of hydrocortisone, and then to inject 1 mgm. of amphotericin diluted with 3 ml. of spinal fluid not more frequently than twice a week. The concentration of amphotericin in the spinal fluid seems to depend more on the level of spinal fluid protein than the amount of amphotericin given by either method. A table is given of the toxic reactions in 18 patients: nitrogen retention occurred in 6 but in only 1 had treatment to be interrupted; 1 infant who received high dosage died with exfoliative dermatitis, purpura, and convulsions; 1 patient died with haemorrhagic gastro-enteritis; otherwise the toxic manifestations were relatively innocuous, though unpleasant.

No reactions followed local instillation. *In vitro* the minimum inhibitory concentration of a number of pathogenic fungi is shown, but the values given by the authors often vary widely from those obtained by other workers. Histories of treated patients who suffered from histoplasmosis, blastomycosis, cryptococcosis and miscellaneous deep mycoses are given. In histoplasmosis, 4 treated by the intravenous route had either prompt healing or considerable improvement; 1 was treated by oral amphotericin without effect. In the blastomycosis group 3 healed promptly with intravenous therapy (2 of these were failures with oral and intramuscular therapy given previously), 1 healed (post-mortem confirmation) but died of intercurrent staphylococcal pneumonia, and 1 was unassessable.

7 patients suffering from cryptococcosis were treated. 1 admitted moribund died on the 6th day; 5 improved on intravenous therapy; 3 of these were treated intrathecally in addition; 1 who had improved on intravenous therapy died after the route was changed to oral because he refused to continue intravenous therapy.

Intravenous therapy was tried on patients suffering from disseminated coccidioidomycosis: 1 improved, but later deteriorated when on lower doses and died in spite of increased dosage, probably because of inaccessible abscesses; 2 with disseminated sporotrichosis were cured. 2 patients suffering from moniliasis were treated, 1 aged 6 months died of toxic reaction, the other died of pyelonephritis after considerable improvement. The dosage and frequency of administration varied unduly, but a dosage of 0·5 mgm. per kgm. of body weight on alternate days is suggested as a start.

[This is a valuable clinical study with good case histories.] *F. H. Young*

DA SILVA LACAZ, C. Aspectos clínicos e epidemiológicos das micoses profundas na América do Sul. [**Clinical and Epidemiological Aspects of Deep Mycoses in South America**] *Mycopathologia.* The Hague. 1959, May 30, v. 10, No. 4, 355–78. [Numerous refs.] English summary.

TEGERIS, A. S. & SMITH, D. T. **Disseminated Pulmonary Histoplasmosis treated with Cortisone and MRD-112.** *Ann. Intern. Med.* 1958, June, v. 48, No. 6, 1414–20, 2 figs. & 1 chart. [17 refs.]

A 32-year-old white male patient from Florida was admitted with what appeared to be acute disseminated pulmonary histoplasmosis some weeks after he had

breathed in dust laden with bat manure while exploring a cave. Severe dyspnoea and cyanosis even with maximal administration of oxygen was ascribed to allergic reaction in the lungs around the infected foci. Administration of cortisone together with a fungicidal drug, beta-di-ethyl-aminoethyl-fencholate (MRD-112) [this *Bulletin*, 1958, v. 33, 234], led to a dramatic relief of symptoms and the patient made a rapid recovery.

Peter Abbott

HIGUCHI, K. & IWASAKI, H. **Systemic Moniliasis complicated with Leukaemia.** *Kyushu J. Med. Sci.* Fukuoka. 1958, Aug., v. 9, No. 4, 139–44, 4 figs.

"In 2 autopsy cases of systemic moniliasis complicated with leukaemia, monilial lesion was recognized in lung, tonsil, intestine and colon in one case, and in lung, bronchus, pleura, spleen, tonsil, esophagus, intestine and colon in the other case. Leukaemia, together with the long-term use of antibiotics is ascribed to the etiologic factor of the disease."

TIANT, F. R. & FUENTES, C. A. Cryptococcosis de localizacion cutanea. [**Cutaneous Cryptococcosis**] *Bol. Soc. Cubana de Dermat. y Sifil.* 1958, June, v. 15, No. 2, 65–72, 2 figs. [18 refs.]

Cryptococcus neoformans infection is not uncommon and it is stated that about 10% of the 300–400 annual deaths from mycoses in the United States are due to it. The authors report a case in a Cuban patient in whom small circumscribed lesions of the skin appeared and spread; they were covered with exudate and were irritating. A photograph shows the body covered with ulcers in a later stage. Eventually a biopsy specimen was examined and intracellular bodies resembling yeast cells were seen in large numbers. They were identified on culture as *C. neoformans*.

The patient was treated with amphotericin B in doses of 0·125–1·0 mgm. per kgm. in glucose solution administered intravenously over periods of not less than 6 hours. This was continued [probably daily] for about 2 months, to a total of 270 mgm. The dosage was only slowly raised from the initial low figure, because the reaction was temporarily distressing, but the result was good and cure was obtained. Earlier treatment with sulphonamide and other medications, before the diagnosis was established, had been ineffective.

Charles Wilcocks

TURNER, P. P. **A Case of Cryptococcosis with Choroidal Torulomata.** *East African Med. J.* 1959, Apr., v. 36, No. 4, 220–23, 2 figs.

AKAGI, M., FUJINO, T., HAYASHI, S., YAMAMOTO, Y. & AKABE, T. **A case of Pulmonary Infection caused by a Black Yeast-Like Fungus.** *Med. J. Osaka Univ.* 1958, Mar., v. 8, No. 4, 585–99, 9 figs.

"A black yeast-like fungus was isolated from the sputa of a patient of pulmonary infection, and considered as the causative agent of this case.

"The fungus was pathogenic against mice, and a positive complement fixation test was obtained with the patient's serum.

"From the results of microbiological examinations it was identified as a variant of *Pullularia pullulans* (de Bary) BERKHOUT."

BRICEÑO MAAZ, T. Caso de muerte por *Nocardia brasiliensis*. [**A Fatal Case of *N. brasiliensis* Infection**] *Gac. Méd. de Caracas.* 1958, Apr.–June, v. 66, Nos. 4/6, 107–9.

The English summary appended to the paper is as follows:—

"A fatal case caused by Nocardia brasiliensis is presented in this paper. The material was collected from the lungs and pericardial sac by the doctors attending the case in Socony Oil Co. Hospital in Anaco, Anzoatgui."

MONTGOMERY, R. M. & WELTON, W. A. **Primary Actinomycosis of the Upper Extremity.** *Arch. Dermat.* 1959, May, v. 79, No. 5, 578–80, 1 fig. [14 refs.]

FINGERLAND, A., SKRIVÁNEK, O., MYDLIL, F. & PROCHÁZKA, J. Plicní aspergilomy. [**Pulmonary Aspergillomas**] *Časopis Lékařů Českých.* Prague. 1959, May 8, v. 98, Nos. 18/19, 550–56.

The English summary appended to the paper is as follows:—

"1. A synthetic study of eight cases of pulmonary aspergilloma, which after a clinical and X-ray examination were operated on and the resection material was examined macroscopically, histologically and bacterioscopically.

"2. Aspergillomas of the lungs do not develop only in bronchiectases [there it developed five times] but also in tuberculous cavities which are about to heal [there it developed twice]. Once it developed in a chronic pulmonary abscess.

"3. The authors make an iconographic correlation of X-ray and macroscopic pictures of aspergillomas."

JENSEN, Magda. Vaginitis mycotica. Behandlingsforsøg i graviditeten med sterosan. [**Mycotic Vaginitis. Therapeutic Trials with Sterosan during Pregnancy**] *Noridsk Med.* 1959, May 14, v. 61, No. 20, 758–60, 1 fig.

The English summary appended to the paper is as follows:—

"Thirty-seven patients with mycotic vaginitis during pregnancy were treated locally with sterosan. In addition, sterosan was administered by mouth in 12 of the cases. All the patients experienced marked subjective improvement, but in practically no case were the fungi killed as the result of treatment."

Rheumatic Diseases

CREA, Maria A. & MORTIMER, E. A., Jr. **The Nature of Scarlatinal Arthritis.** *Pediatrics.* Springfield, Ill. 1959, May, v. 23, No. 5, 879–84. [15 refs.]

"In order to determine the relationship of scarlatinal arthritis to rheumatic fever, 18 patients who experienced joint symptoms early in the course of scarlet fever were interviewed and examined 1 to 20 years later to establish the incidence of subsequent rheumatic symptoms.

"Two patients experienced definite pancarditis during the original illness, and the course of the arthritis in two additional cases was highly suggestive of rheumatic fever. Subsequent stigmata of rheumatic fever appeared in six other patients. Thus, the episode of scarlatinal arthritis probably represented rheumatic fever in eight instances, and possibly in two more.

"It is concluded that scarlatinal arthritis is most likely a manifestation of rheumatic fever."

ILLINGWORTH, R. S., LORBER, J., HOLT, K. S. & RENDLE-SHORT, J. **Acute Rheumatic Fever in Children. A Comparison of Six Forms of Treatment in 200 Cases.** With a Statistical Addendum by G. H. JOWETT & Wendy M. GIBSON. *Lancet.* 1957, Oct. 5, 653–9. [14 refs.]

This article presents an analysis of the results of treatment of 200 children suffering from rheumatic fever during the last 9 years in the University of Sheffield Department of Child Health. No drug treatment was given to 42 children and the others received either high or low dosage salicylate treatment or cortisone alone or combined with high or low dosage salicylates. Cortisone combined with salicylates, especially in high dosage, was the most effective treatment: cortisone alone was better than salicylates and salicylates were better than no treatment. The results were the same whatever the criterion—fall in ESR, fall in temperature, disappearance of arthritis, disappearance of cardiac signs, duration of treatment and stay in hospital. New rheumatic manifestations did not develop in the cortisone groups but did in all other groups. The authors are convinced that treatment of rheumatic fever without cortisone is inadequate treatment and that all children with rheumatic fever should be treated in hospital with combined therapy and preferably within 30 days of the onset of symptoms. [The data have been subjected to full statistical analysis: for details of this and of treatment schedule reference to the article is essential.] *A. B. Christie*

ILLINGWORTH, R. S., with statistical assistance from G. H. JOWETT & Wendy M. GIBSON. **Cortisone Treatment of Rheumatic Fever. Relationship of Weight to the Speed of Fall of Erythrocyte-Sedimentation Rate.** *Lancet.* 1957, Oct. 5, 659–60.

In a group of children being treated for rheumatic fever it was noted that when cortisone was used, with or without salicylates, the erythrocyte sedimentation rate returned more slowly to normal in the overweight than in the underweight children. When salicylates without cortisone were used the difference favoured the overweight group but was not statistically significant. These observations are thought to indicate that the 2 drugs act differently and to be a reason for using both drugs in the treatment of rheumatic fever.

A. B. Christie

MCCUE, Carolyn M. **Steroid Therapy for Rheumatic Fever.** *J. Pediatrics.* St. Louis. 1957, Sept., v. 51, No. 3, 255–61.

This article describes the treatment with cortisone or prednisone of 94 children suffering from rheumatic fever. There were 4 schemes of treatment—cortisone 150 mgm. daily for 21 days, 200 mgm. for 14 days tapering to 61 days, 300 mgm. for 21 days tapering to 61 days and prednisone 60 mgm. daily tapered to 61 days. There are no control groups and the 4 groups were treated at different times. The most common problem was the rebound phenomenon. The authors were satisfied that the drug, especially in high dosage and when started early in the disease, was beneficial and sometimes life-saving. [In the absence of untreated or salicylate treated controls the author's conclusions consist only of clinical impressions.] *A. B. Christie*

WOOD, H. F., STOLLERMAN, G. H., FEINSTEIN, A. R., HIRSCHFELD, Ilse, RUSOFF, J. H., TARANTA, A., HAAS, R. C. & EPSTEIN, Jeanne, A. **A Controlled Study of Three Methods of Prophylaxis against Streptococcal Infection in a Population of Rheumatic Children. I. Streptococcal Infections and Recurrences of Acute Rheumatic Fever in the First Two Years of the Study.** *New England J. of Med.* 1957, Aug. 29, v. 257, No. 9, 394–8. [23 refs.]

A total of 405 children all with a definite history of rheumatic fever within the preceding 28 months were given one of 3 prophylactic treatments over a period of 2 years—sulphadiazine 1 gm. once daily by mouth, penicillin 200,000 units once daily by mouth, and benzathine penicillin G 1,200,000 units by intramuscular injection once every 4 weeks. As judged by the incidence of streptococcal infections or the recurrence of rheumatic fever the injection of penicillin was superior to the other 2 methods. The reason may well have been the failure of the children on oral prophylaxis to take their drug regularly. *A. B. Christie*

FEINSTEIN, A. R., WOOD, H. F., EPSTEIN, Jeanne A., TARANTA, A., SIMPSON, Rita & TURSKY, Esther, with the collaboration of T. ARGYROS, J. FRIEDEN, R. C. HAAS, Ilse HIRSCHFELD, A. J. LEWIS, C. MANSO & K. ULICH. **A Controlled Study of Three Methods of Prophylaxis against Streptococcal Infection in a Population of Rheumatic Children. II. Results of the First Three Years**

of the Study, including Methods for evaluating the Maintenance of Oral Prophylaxis. *New England J. of Med.* 1959, Apr. 2, v. 260, No. 14, 697–702.

Prophylaxis against streptococcal infection was carried out in 391 children and adults with previous attacks of rheumatic carditis by one of 3 methods—1,200,000 units of benzathine penicillin G given once monthly by injection, potassium penicillin G 200,000 units once daily by mouth, or sulphadiazine 1·0 gm. daily by mouth. In the suppression both of rheumatic relapses and streptococcal infection penicillin by injection proved best. Sulphadiazine was at least as good as penicillin by mouth. The incidence of streptococcal infection per patient year was 21·1% for sulphadiazine, 20·7% for oral penicillin and 7·3% for penicillin by injection: the incidence of rheumatic fever per patient year was for sulphadiazine 1·9%, for oral penicillin 5·0%, and for penicillin injections 0·3%.

A. B. Christie

Cancer

World Health Organization. Technical Report Ser. No. 164. **Expert Committee on Health Statistics. Sixth Report including Third Report of the Sub-Committee on Cancer Statistics, Geneva, 29 September–4 October 1958.** 43 pp. [Refs. in footnotes.] 1959. Geneva: Palais des Nations. [Sales agent for U.K., H.M. Stationery Office.] [1s. 9d.; $0.30; Sw.fr. 1.–.]

Meeting in Geneva in the autumn of 1958 under the chairmanship of Dr. W. P. D. Logan, Chief Statistician to the General Register Office of England and Wales, the Expert Committee on Health Statistics gave special attention to terms and measurements in the field of morbidity statistics. They make recommendations regarding the basic measurements of (1) the frequency of illnesses commencing during a defined period (incidence); (2) the frequency of illnesses in existence at any time during a defined period (period prevalence); and (3) the frequency of illnesses in existence at a particular point of time (point prevalence). They discuss the applicability of these basic measurements to general surveys of sickness, hospital in-patient statistics, notifications of disease, industrial sick-absences, and social security morbidity statistics. They recommend that the concepts, definitions and terms that they have set out under these various headings be adopted for the national and international presentation of morbidity statistics.

They would like to see the usefulness of survey methods for public health planning more intensively studied.

Under long-range programmes in vital and health statistics they consider planning for the Eighth Revision of the International Classification of Diseases and specially recommend early preparatory work and critical appraisal of its results on 3 sections: (1) the causes of stillbirth, (2) mental, psychoneurotic and personality disorders and (3) cardiovascular diseases. They reviewed the activities of national committees on vital and health statistics and deplored the fact that only 35 of the 88 members and associate member states of WHO had established one.

In considering the epidemiology of cancer the Committee underlined the statistical competence required for such studies and believed that statistical advice and assistance must be available at all stages from planning to evaluation and publication of results. In more detail the Sub-Committee on Cancer Statistics sets out some very useful comments and ideas on methods for measuring the incidence and prevalence of cancer, a registration system, epidemiological and geographical aspects of the disease, the statistics of the results of treatment, clinical staging and the accuracy of diagnoses on death certificates.

A. Bradford Hill

General Register Office. **Studies on Medical and Population Subjects No. 13. Cancer Statistics for England and Wales 1901–1955. A Summary of Data relating to Mortality and Morbidity** [McKenzie, A., with additional material by R. A. M. Case & Joan T. Pearson]. pp. iv + 99. 1957. London: H.M. Stationery Office [5s. 6d.]

The annual publications of the General Register Office of England and Wales invariably contain much detailed information on mortality from cancer. For easy reference this present volume brings together the more important data which were published during the years 1901–55. Thus for many different sites of cancer it includes standardized rates, rates by sex and age, and rates by geographical areas. It also includes, from data collected under the National Cancer Registration Scheme, survival rates for selected sites, according to sex and clinical stage. A short text draws attention to some of the salient features. An appendix to the report contains a set of mortality tables compiled by Case and Pearson of the Chester Beatty Institute of Cancer Research which illustrate in very considerable detail the changes that have taken place in cancer mortality of different sites and at different ages during the past 45 years. They are invaluable for anyone wishing to undertake a comparative cohort analysis, *e.g.* to compare the deaths recorded in an industry with those that would be normally anticipated.

A. Bradford Hill

LEGUÉRINAIS, J. & MAUJOL, L. La mortalité par cancer en France en 1957. [**Deaths from Cancer in France in 1957**] *Bull. Inst. Nat. Hyg.* Paris. 1959, Jan.–Feb., v. 14, No. 1, 33–63, 5 graphs & 4 maps.

In France the number of deaths from cancer has risen rapidly during recent years. The number of deaths in 1957 as a percentage of the number in 1936 was 236 for males and 176 for females and the rise in the standardized death-rate was 212 and 151, respectively. The method of standardization was that of an average equivalent death-rate, and was the unweighted average of the death-rates in 18 quinquennial age-groups, ages 85 + being taken as a five-year group. In 1957 the male death-rate from cancer was larger than the female rate in each 5-year age-group except 30–34, 35–39, 40–44 and 45–49. The percentage of the total cancer deaths that occurred after the age of 65 was 55·8 for males and 62·3 for females. For the major sites, buccal cavity and pharynx, digestive system, respiratory system, breast, skin and uterus, the death-rates and the proportion of the total deaths due to cancer in each age-group are shown for 1948, 1953 and 1957. For 12 lesser sites the death-rates and proportion of cancer deaths are given for 1957 only. The death-rates from cancer are given for each department of the country for the 3 years 1948, 1953, and 1957 and for the large towns for 1957. *W. J. Martin*

POSNER, E., MCDOWELL, L. A. & CROSS, K. W., with the co-operation of G. P. BARDSLEY, A. G. EVANS, J. T. HUTCHISON & R. J. POSNER. **Mass Radiography and Cancer of the Lung.** *Brit. Med. J.* 1959, May 9, 1213–18, 1 chart. [35 refs.]

The value of mass radiography as a method of reducing mortality from cancer of the lung is disputed. This paper deals with 238 out of 240 male cases found by the Birmingham mass radiography unit in the 12 months from July 1, 1955. It is unlikely that there were many mis-diagnoses.

Of subjects referred by general practitioners, 8·7 per 1,000, and of routine surveys 0·3 per 1,000, were found to have cancer. The results in the various age-groups show similar proportions between the two series.

Irrespective of treatment, survival at the end of 1 year was 50% in the routine, and 36% in the general practitioner group, but the difference is not statistically significant. 43·8% of the routine and 30% of the general practitioner cases were deemed resectable. It was noted that two-thirds of the patients were referred by their general practitioners within 2 months of the first consultation. A higher proportion of the cases deemed resectable had a gap of 3–4 months between first consultation and X-ray than those referred in less than 2 months. Only 7 cases were found to be entirely asymptomatic; of these 4 were resectable. A note reports that at the end of 2 years 20% of those referred by general practitioners and 25% of the routine cases were alive.

It is concluded that although some advantage accrues from the use of routine mass radiography it has not, as used at present, a great advantage over a free X-ray service for general practitioners in reducing the death-rate from pulmonary carcinoma. *F. H. Young*

FRIBERG, L., KAIJ, L., DENCKER, S. J. & JONSSON, E. **Smoking Habits of Monozygotic and Dizygotic Twins.** *Brit. Med. J.* 1959, Apr. 25, 1090–92.

Study has been made of 59 pairs of monozygotic twins and of 59 dizygotic pairs matched with them for age and sex. They were classified as regular smokers, sporadic smokers and other non-smokers. Of the monozygotic group 45, or 76%, belonged to the same smoking group compared with 34, or 58%, of the dizygotic group. In other words there was a significantly greater concordance in the former group. This may well be due to a constitutional factor though a more uniform environment with monozygotic twins cannot entirely be ruled out.

[An accompanying leading article points out that even accepting a genetic factor as the whole explanation of the quite small difference there is still no evidence of hereditary factors in lung cancer. Moreover a genetic explanation of the cigarette smoking/lung cancer association fails to account for the rise in mortality of recent years and for the fall in mortality that follows stopping smoking. It also ignores the experimental evidence that tobacco tars contain carcinogenic agents.] *A. Bradford Hill*

NORGAARD, A. **Tobacco Consumption in Denmark. III. The Danish National Morbidity Survey of 1950. Communication No. 15.** *Danish Med. Bull.* 1959, Mar., v. 6, No. 2, 54–8, 1 fig.

The organization and principal results of the Danish national survey of smoking habits have been reported previously (HAMTOFT and LINDHARDT, *Danish Med. Bull.*, 1955, v. 2, 213; 1956, v. 3, 188). The present paper reports (1) the influence of the war on the age at starting to smoke and (2) changes in smoking habits as a result of the publicity given to the relationship between lung cancer and smoking.

Questions were asked about the age at which present smokers or ex-smokers first began to smoke. The data have been analysed to show the proportion of non-smokers at the beginning of each 5-year period who began to smoke during that period and figures are given separately for men born in each quinquennium from 1890–4 to 1935–9 and for women born in quinquennia from 1900–4 to 1935–9. The results show that there has been a progressive increase in the proportion of women beginning to smoke in each age-group but there has been little change in the proportions of men. During the war more women began to smoke than would have been expected in nearly all age-groups; no effect was detected among men, except that there appears to have been an increase in the proportion beginning to smoke at ages centred round 21 years.

Among 4,260 men and 2,089 women who said that they had been smokers immediately before the publicity on lung cancer (*i.e.* the latter part of 1953), there were 158 men (3·7%) and 90 women (4·3%) who said that they had changed their habits as a result of the

discussions. Among these, 13% and 11% had stopped smoking entirely. The majority of the women who changed had reduced their consumption of tobacco but had not changed from cigarettes. Among the male cigarette smokers, however, about one-half had changed to cigars, cigarillos or a pipe. The survey was conducted at the beginning of 1954 and the changes in habit may not have persisted. *Richard Doll*

BROWN, W. M. C. & DOLL, R. **Adult Leukaemia. Trends in Mortality in relation to Aetiology.** *Brit. Med. J.* 1959, Apr. 25, 1063–9, 5 figs. [12 refs.]

The deaths attributed to leukaemia in England and Wales in 1945–9, 1950–4 and 1955–7 have been distributed to 3 groups *viz.* chronic lymphatic leukaemia, chronic myeloid leukaemia and acute leukaemia. In carrying out this division the proportions of acute and chronic cases in those in which the type was not described on the death certificates have been divided in the same proportions as those at each age in which the type was described. On this assumption age specific death rates of men and women have been calculated and their trend in time examined. All 3 types of leukaemia show an increase in old age but at ages under 60 years the only striking rise is in the acute form. At least some part of the increase in old age is likely to be due to more detailed and more accurate death certification—and deaths attributed to senility have fallen appreciably in England and Wales over the 13 years in question. The data for acute leukaemia, on the other hand, suggest an increase in mortality of approximately one-third at all ages under 65 years and in both sexes and it seems reasonable to regard this as a real change in incidence and one due to increasing exposure to some leukaemogenic factor in the environment. Ionizing radiation is the only leukaemogenic agent for which there is convincing epidemiological evidence in man and it is one to which the population has been increasingly exposed. The present data are therefore compatible with the concept that this increased exposure has played some part in the changed incidence of the disease.

A. Bradford Hill

Miscellaneous Diseases

ŽARKOVIC, G. & RADOVANOVIC, M. **Extent and Epidemiology of Endemic Goitre in Bosnia and Herzegovina.** *Bull. World Health Organization.* Geneva. 1958, v. 19, No. 6, 953–65, 1 map.

A short outline of the records of endemic goitre prevalence in Bosnia and Herzegovina from as far back as 1878 introduces the description of a survey of the disease carried out in the summer months of 1956 with support from the Central Institute of Hygiene of Bosnia and Herzegovina. The territory of these areas contain 195 counties, each of which was divided into 5 segments and about 1% in all age-groups over the age of 6 years were examined. This sample contained 34,343 persons among the 3,084,000 of total population of whom 2,517,665 were 7 years old and over. The 3-stage classification of thyroid enlargement put forward by the WHO Study Group on Endemic Goitre (*Bull. Wld. Hlth. Org.*, 1953, v. 9, 293) was adopted. Samples of water were taken from every settlement covered in the survey and sent for chemical analysis.

Table I of the results of survey gives the number of persons with goitre by age, sex and degree of thyroid enlargement. A high incidence of goitre—290·3 per 1,000 of the total surveyed population was found. Signs of goitre were found in 1 in 5 males and a little more than 1 in 3 females, a sex difference which was most marked after adolescence. The goitre rate increases with age in both sexes up to the fifth decade of life, after which it gradually decreases.

Goitre morbidity was statistically analysed by religious group—Serbian Orthodox, Moslem and Roman Catholic—as these groups largely coincide with ethnical grouping and the results were that goitre was much less prevalent among the Roman Catholics than among the other 2 religious groups.

The great variation in goitre incidence in the different counties is described with an illustrative map.

The chemical data on the iodine content of the many water samples are set out in tables in relation to goitre prevalence, by stage of the disease and according to the altitude of the settlements surveyed.

There is a discussion of the results of the whole survey. In relation to the iodine values it is stated "The failure of our investigation to discover any positive correlation between the quantity of iodine in the drinking-water and the prevalence of goitre cannot be taken as proof that lack of iodine is not the most important single agent in the epidemiology of goitre."

M. E. Delafield

Occupational Hygiene

In this section the abstracts are arranged as far as possible in the following order: General; Mining and Dust Diseases; Poisoning due to Metals, Solvents and Other Substances; Skin and Other Affections; Radio-Active Substances; Other Conditions; Occupational Psychology

INTERNATIONAL LABOUR OFFICE. **International Directory of Institutions engaged in Study, Research and other Activities in the Field of Occupational Safety and Health.** Vol. I. A–I. Vol. II. J–Z. Numerous mimeographed pp. 1958. Geneva.

This Directory, in mimeographed form, relates to institutions in the field of occupational safety and health and is arranged alphabetically by countries. The details of each institution, obtained by questionnaire, include name (in the original language and in English, where appropriate), address, status (*e.g.* government department, private foundation), principal functions, research and other activities, and publications.

The number of institutions and the level of work achieved by them depend on the extent of industrialization of the country concerned and have influenced accordingly the selection of national institutions for inclusion in the Directory. For highly industrialized countries, it has been necessary to restrict the choice to representative examples of the many types of institutions set up by national, state and municipal authorities, research organizations, private industry, insurance companies, etc.

This publication should become a useful work of reference to facilitate exchange of information and co-operation among the institutions. The loose-leaf form of the Directory, although rather cumbersome, will allow for expansion and amendment. [In this latter respect, inclusion of names of directors of institutions and of departments, rather than of office titles alone, will cause unnecessary work, since the information in several instances is already out of date.]

A. H. Phipps

MINISTRY OF LABOUR & NATIONAL SERVICE. **Duties, Organisation and Staffing of the Medical Branch of the Factory Inspectorate.** Cmnd. 736. 11 pp. 1959, May. London: H.M. Stationery Office. [9d.]

4 senior members of the Ministry of Labour including the Chief Inspector of Factories and the senior Medical Inspector of Factories have reviewed the duties, organization and staffing of the medical branch of the Factory Inspectorate. This White Paper reports on the survey and states the decisions reached by the Minister.

The medical establishment numbers 18 (5 posts are at headquarters). Their duties include visits to factories to study and advise on conditions of work and collaborating with other members of the inspectorate to enforce the Factories Acts. It has been suggested that their work be broadened to take in duties in connexion with military recruitment, Government Training Centres, youth employment and disabled persons. Such a change is not considered desirable except in relation to disabled persons. The view that there should be a substantial increase in the number of medical inspectors is not endorsed.

No change is recommended in staffing arrangements other than that 1 more medical inspector be appointed to meet the increase in the divisions from 13 to 14. A few paragraphs are devoted to the recruitment and training of medical staff. Again no great change from past practice appears likely.

Finally, in view of the need for collaboration and for single responsibility, the suggestion that the medical inspectorate be directly responsible to the head of the Safety, Health and Welfare Department in place of the Chief Inspectorate of Factories, is rejected.

In brief there is to be 1 more medical inspector, the doctors are to be better supplied with books and equipment and they are to take slightly more interest in disabled persons. Otherwise things are to remain substantially as they have been for many, many years.

T. O. Garland

SLOUGH INDUSTRIAL HEALTH SERVICE. **Tenth Annual Report 1956–1957 and a Review of the First Ten Years.** 76 pp., 9 figs. (1 folding). 1958. Slough: Community Centre, Farnham Road, Bucks.

The Tenth Annual Report reviews the development of the Service: full of information, it tells of ideals achieved and common-sense adaptation. This experimental unit of a group of manufacturers, each employing from 5 to 1,500 workers, sponsored by The Nuffield Foundation, The Nuffield Provincial Hospitals Trust and Slough Estates Limited, was registered as a non-profit-making limited company with charitable objects. Its aim was to meet the industrial health needs of urban workers in large and small firms in the Slough area, near London. It was asked that facilities should be provided for the investigation and control of hazards in the working environment and for the rehabilitation and resettlement of workers after injury or illness, that liaison should be established with an academic body and that the Service should form an integral part of the general health services of the community. The Council of Management was formed of representatives of management, the Slough Trades Council, the Ministries of Labour and Health and the University of London.

The original basic organization remained: a central clinic; 2 dressing stations for factories farther away; a mobile dressing station; medical departments in 5 large firms (and since 1954 in the Ministry of Labour's Government Training Centre); a residential rehabilitation centre at Farnham Park for short-stay cases from

industry and hospitals [but see below]; out-patient facilities at the central clinic shared with the Canadian Red Cross Memorial Hospital and some of its consultant staff appointed part-time consultants to the Service. After a generous response to an appeal in 1954, the central clinic was extended and equipped at a cost of £60,000. It has: a casualty department with theatre for minor operations; eye, X-ray, physiotherapy, chiropody and records departments; an occupational hygiene department with sound, dust and general laboratories; a gymnasium and lecture hall; consulting rooms, administrative offices, staff canteen, etc.

Membership of the Service increased from 52 firms with 6,324 employees to 179 with 17,748. All known industrial hazards to member firms have been investigated and controlled. First-aiders have been trained and equipped. Liaison has been maintained with general practitioners, hospitals, chest clinics and the Ministry of Labour and Factory Inspectorate. The units work under the direction of 4 full-time medical officers who also act as part-time works medical officers to the medical departments of the 5 large firms who employ their own nurses. The other factories are divided into 4 groups, each group supervised by a Service nurse, her routine treatment being governed by administrative orders. The emergency team is on call at the central clinic. The cost of the full service to the firms with no medical departments, employing 11,500, is £2 per head per annum, and of the casualty service only, 20s. 6d. (the latter figure includes also the doctors' work at the central clinic for employees of firms with their own casualty stations or medical departments).

The casualty service supervises 500 cases daily, 98% being able to continue work after treatment; the mobile dressing station treats over 2,000 cases annually, average time 5 minutes. A relative decrease in the attendances at the clinics may be partly due to the preventive measures advised. The ratio is 3·2 attendances to each new case. 40% of the attendances are for occupational causes, with little variation in their proportion. Industrial eye injuries are 12% each year, though education may have caused more workers to report recently, and there is a proof that complications after eye injuries have been reduced. Orthopaedic, hand injury and skin clinics are held weekly.

Medical examinations numbered 24,790 in the 10 years, with an increase in the proportion requested by management and individuals. Voluntary examination of senior executives led one firm to employ more junior managerial staff, with a decline in the seniors' symptoms. The trainees at the Government Training Centre, 40% of whom are disabled, naturally had a high attendance rate; in 1956 there were 4,000 attendances among an average population of 354.

When the physiotherapy department started, many juveniles entering industry were referred by the Appointed Factory Doctor (AFD) for treatment of postural deformities. The service offered its facilities to the Education Authority and increasing numbers of schoolchildren were referred by the School Medical Officers. The Education Authority then took over this work and the cases from the AFD dwindled and ceased. One-half the patients now are referred by the hospitals, and though the proportion of industrial workers among them is high, they do not necessarily belong to member firms. In a year about 1,600 new patients attend for 20,000 treatments: the cost 6s. 1d. a head.

The occupational hygiene service, formed in 1949 with laboratories at the London School of Hygiene and Tropical Medicine, has been transferred to the new central clinic buildings. About 56 major investigations have been completed and a report sent to the firm concerned. Member firms will continue to have priority: cost 2s. 11d. a head. In future this service will be extended beyond the area and this will be charged for.

Farnham Park accommodates 66 in-patients and 30 out-patients; 5,113 have been treated, 40% from nearby hospitals and the remainder from other areas, and 70% have been able to return to former or similar employment. In 1956, of 677 admissions, 508 were able to resume work and arrangements were made for 40 to be retrained. One-half the patients need physiotherapy; 2,465 treatments 10 years ago increased to a maximum of 19,902 in 1955–6. The therapeutic pool provided in 1952 has been used for 5,000 treatments each year under the supervision of the physiotherapy and remedial gymnastic departments. The occupational therapy department, now the basic one, has, however, limited its range of manufacture: it was impracticable to continue the type which was of value in restoring fine hand movements because of the individual training, and contract work for member firms was given up because, among other reasons, patients who did not need that work for therapy were employed to finish the contracts. The social service department formed in 1951 deals more with the future employment of Farnham Park patients than with employees of member firms, some of whom appear unaware of its existence though visits have been made to some factories and employees' homes. The cost of Farnham Park for the last year was nearly £44,000, £34,000 of it being paid by the Regional Hospital Board. The Service can no longer accept financial responsibility for Farnham Park and its future is under consideration by the Regional Board.

Until 1952 when it was closed, The Nuffield Bureau of Health and Sickness Records at Oxford was responsible for the supervision and analysis of the records of the Service. Based as they always were on the patient-unit system, records, whether for clinics, medical departments or Farnham Park, are controlled, filed and analyzed by the Records Office at the central clinic. The basic document is a chronological "Casualty" card with a record of every attendance at any department. For the periodic statistics, general for the service exemplified in the report and specific for each firm, casualty figures are taken from loose-sheet note books kept by the nurses, and figures for medical examinations from transcription sheets. The statistics give information necessary for day-to-day administration and for future planning.

The cost of the comprehensive industrial health service over the year 1957, excluding Farnham Park, was £26,000; but if the cost of the 4 doctors, nurses and incidental expenses had been borne by the service instead of partly by Farnham Park, the figure would have been £29,000; the cost of firms with no medical

departments was £23,000 and £6,000 represents the average cost of the full service to the 5 firms and the Government Training Centre.

(The Eleventh Report for 1957–8 shows a few changes: population, 11,394; professional supervision of 134,000 attendances at all clinics including medical departments of firms; eye injuries decreased from 1,521 to 1,388; nurses have been allowed to treat a higher proportion on their own responsibility; at Farnham Park administrative arrangements have been made by which it could be a self-contained unit if acquired by the National Health Service, and a new records department has been set up there and all records transferred from the central clinic.) *M. Patricia Fitzsimons*

TAYLOR (Lord). **Harlow Industrial Health Service. Lessons of an Experiment in Industrial Co-operation.** *Lancet.* 1959, Apr. 25 & May 2, 875–80; 933–6, 6 figs. [Refs. in footnotes.]

In this new town the comprehensive facilities provided by this kind of industrial health service, valuable for small and medium factories, depended for success on initial financial support, careful costing and complicated administration, and also mobility of doctors and nurses. Planned in 1954 and started in 1955, the main pattern follows that of the Slough Industrial Health Service [see above] except that hospital functions were not undertaken and the general practitioners, who already ran the principal local authority clinics, are the medical officers. The first object was to achieve prompt treatment of accidents and illnesses occurring at work, as an essential step in propagating the larger aims of industrial medicine.

A 24-hour service to 40 firms employing nearly 6,000 workers costs full member-firms £2, and those employing their own nurses £1, per employee annually. Building firms, whose employees are at risk, numerous and difficult to arrange for, may become associate members subscribing either 1 shilling per £100 value of the contract spread over its duration or £1 per week per site. The Industrial Health Centre, capable of serving 10,000 workers, replaced a temporary building in 1957. It cost £18,600 including furnishing and a hut extension, and another is planned for Harlow's second industrial estate. Assuming 15,000 workers in future, the initial capital expenditure, borne by the Nuffield Provincial Hospitals Trust, will have amounted to about £2 per worker and the initial subsidy to less than £1 10s.

During his 4-hour morning or afternoon session, one of the 10 doctors is on emergency call and at prearranged times visits the Centre and his factories. Night and week-end emergencies are shared by 2 doctors. Each session is treated notionally as lasting for 2 hours at British Medical Association rates. A nurse drives a waggon to each factory daily to treat appropriate cases. First-aiders have been trained and first-aid boxes are equipped from the waggon, which is also used to transport patients. 2 nurses, a receptionist-telephonist, 3 part-time nurses and the medical director, the secretary-administrator and the typist, who also work part-time, complete the staff. Some pre-employment examinations are carried out on request. Orthopaedic and dermatological clinics are held monthly. An ophthalmologist, an optician, a physiotherapist and a chiropodist are in attendance, and 18 member-firms pay £2 2s. for each voluntary examination of senior executives by a physician. Emergency treatment of non-members has been given and the chief problem is to increase membership. *M. Patricia Fitzsimons*

HARADA, T. & FUKUHARA, K. **On the Hazards of Upper Extremities caused by Portable Pneumatic Tools—especially on X-Ray Findings of Workers' Elbows.** *Kobe J. Med. Sci.* 1958, Sept., v. 4, No. 3, 179–84.

This article records the results of examining 22 rivetters and 16 holders. More than 50% gave a history of numbness, pain and blanching of fingers with stiffness of the joints. These symptoms were more common in winter time and were most noticeable after going to bed. The elbows were X-rayed in 14 men. In 3 of the rivetters who had been over 15 years in the job the head of the radius showed a distinct bony change (osteohyperplasy), only very slight changes were discernable in the others. *T. O. Garland*

LAWRENCE, J. S. **The Problem of Rheumatism in Industry.** *Trans. Ass. Indust. Med. Officers.* 1959, Apr., v. 9, No. 1, 22–9, 9 figs. [12 refs.]

This paper submitted at a joint meeting with the Empire Rheumatism Council in October, 1958 contains a discussion of the problem of rheumatism in industry with particular reference to published surveys of rheumatism in miners [this *Bulletin*, 1952, v. 27, 667, 1121; 1956, v. 31, 40] the results of which are compared with the findings in some studies of rheumatic diseases in the general population. The data from National Health Insurance experience in the year 1953–4 were that the most important cause of loss of work from sickness and accident was rheumatism with a loss of 28,000,000 days. Included in the term rheumatism were—"rheumatism as such, rheumatic fever, arthritis, displacement of intervertebral discs, synovitis, bursitis and tenosynovitis, ankylosis and acquired musculo-skeletal deformities, gout and sciatica".

The amount of incapacity from arthritis and rheumatism is much greater in the mining and quarrying industry than in other occupations. The studies on miners indicate that the types and conditions of their work are responsible for some of this incapacity and it would appear that "The heavy toll of rheumatic disease in miners is clearly preventable".

The lessons learnt from studies on miners are not to be applied to other industries without further investigations. To obtain more adequate background information on the general incidence of rheumatism "a number of surveys are in progress using random samples of the population". Some of the finding of these surveys are here discussed from the clinical and therapeutic point of view. Finally stress is laid on the fact that although physiotherapy may reduce the period

of incapacity in some of the occupational forms of rheumatism, it "cannot affect the underlying disease".

M. E. Delafield

McCord, C. **The Zooanthroponoses as Occupational Diseases in the United States.** *Indust. Med. & Surgery.* Miami. 1959, Apr., v. 28, No. 4, 165–73.

Though about 150 zoonoses are now recognized, any of which occur occupationally, physicians in the United States of America have been very slow to accept them as occupational diseases. Many have been known a long time, have been regarded as ordinary diseases, and only recently has their occupational character been realized. For a variety of reasons there are no official statistics showing the frequency of zoonoses as occupational diseases. This article reports that the lowest reported incidences of zoonoses are in States with few veterinary facilities, and it must be assumed that the real incidence is equal to or greater than that reported in areas where veterinary skills are highly developed. The 10 zoonoses which occur most commonly as occupational infections in the United States are brucellosis, psittacosis, erysipeloid, mycoses, parasitic infections, Q fever, tularaemia, mite dermatitis, anthrax and leptospirosis. The professions and occupations of persons occupationally exposed to these diseases are listed. There have been few instances of compensation being paid for zoonotic infection contracted occupationally. The legal difficulties relating to compensation for such infections are considered and it is thought desirable that exacting criteria should be applied. Part of the paper is devoted to descriptions of a variety of conditions which might have been referred to an industrial physician, some of which simulated and some were zoonoses contracted in occupation. Eradication of the zoonoses is the responsibility of the veterinary profession but their control as occupational infections needs the cooperation of the medical profession.

T. H. Davey

Bidstrup, P. Lesley. **Occupational Causes of Lung Cancer.** *Trans. Ass. Indust. Med. Officers.* 1959, Apr., v. 9, No. 1, 2–4. [24 refs.]

Marks, J. & James, Dinah M. **The Measurement of Dust Toxicity** *in vitro. J. Path. & Bact.* 1959, Apr., v. 77, No. 2, 401–6.

Marks and Mason in 1956 [this *Bulletin*, 1957, v. 32, 47] described a method of measuring the toxicity of different dusts on macrophages *in vitro*. Subsequent experience showed that the method lacked precision. An improved technique has now been devised, the basis of which is that toxicity of the dust is measured by its power to depress the metabolism of macrophages in tissue culture. 3 measurements of tissue metabolism are used; oxygen utilization, glucose consumption and dehydrogenase activity. The last, determined by the reduction of tetrazolium, proved to be the most useful measure of toxicity.

A. Meiklejohn

Mosinger, M., Fiorentini, H., El Feki, M., Cartouzou, G., Bouisson, Gras, A. & De Bischop, G. Le syndrome biochimique général chez les animaux silicotiques. Le cas du chien. [**The General Biochemical Syndrome in Silicotic Animals. The Picture in the Experimental Dog**] *Arch. Malad. Professionnelles.* Paris. 1958, Nov.–Dec., v. 19, No. 6, 549–63.

One group of the dogs received quartz powder by intrabronchial injection, a second group received quartz suspended in serum by intrabronchial injection and a third group received quartz, also suspended in serum, but by intra-abdominal injection. Total serum protein and serum albumin were estimated quantitatively and the serum albumin, globulins, amino-sugars and lipids were separated by electrophoresis. This was done at different dose levels of quartz and at different time intervals. In one group serum cholesterol, both total and esterified, and serum glucose were also estimated.

The results showed a general reduction of albumin and increase of γ globulins either earlier or later after injection of quartz. There was an increase of α 2 globulin in those animals which received a high dose of quartz and showed symptoms of shock. The increase of γ globulin occurred later in these animals. In the animals which received only a small dose of quartz increase of γ globulin occurred very soon after injection. At the end of treatment there was considerable reduction in α 2 globulin while α 1 globulin retained its normal value or increased slightly. Amino-sugars increased in parallel with the γ globulins and were associated with the α and γ fractions. The β lipoproteins increased later as the α decreased. In time albumin slowly regained the normal level but γ globulins and β lipoproteins remained increased. In the dog there is variable elevation of serum cholesterol after administration of quartz. Blood sugar levels were markedly reduced after injection of high doses of quartz and the changes were more marked in those animals which received quartz by the intra-abdominal route.

The dog is suggested to be a more suitable experimental animal for the study of silicosis since it is more easy to assess the general biological changes in the whole animal. [Similar results have been obtained with the more common and smaller laboratory animals.]

D. Rivers

Gross, P. **Silicosis: a Critique of the Present Concept and a Proposal of Modifications.** *Arch. Indust. Health.* Chicago. 1959, Apr., v. 19, No. 4, 426–30, 2 figs. [18 refs.]

The migration of inhaled dust particles within the lungs is still a matter of controversy. The subject has been complicated by recent studies which suggest that the so-called perivascular space and intrapulmonary lymphoid tissue do not exist under normal conditions. The author submits that the present "old" concept of the migration of dust-laden macrophages, involving a variety of positive and negative tropisms, is inadequate. He advances his own "new" interpretation.

The "old" and "new" concepts are represented schematically as a flow chart. These diagrams are complicated and must be studied in the original article.
A. Meiklejohn

MARKS, J. **Further Studies of the Neutralization of Silica Toxicity** *in vitro*. *Brit. J. Indust. Med.* 1959, Apr., v. 16, No. 2, 166–9.

Compound 48–80, a drug used in experimental pharmacology to release histamine from mast cells, was shown by Marks [this *Bulletin*, 1958, v. 33, 592] working in the Central Tuberculosis Laboratory, Cardiff, to have the power to protect phagocytic cells against injury by silica dust. This was proved by experiments on tissue cultures and thereafter in mice. Unfortunately only very small amounts of this drug are tolerated by man. In this situation certain related compounds were investigated to determine whether the properties of histamine release and the neutralizing action on silica are distinct. The experiments were *in vitro* with tissue cultures according to the dehydrogenase technique [MARKS *et al.*, *ibid.*, 1959, v. 34, 348]. Among the compounds tested 46–107 appeared to be relatively harmless to mast cells, and effective against the effect of silica dust.

Other substances found to neutralize the toxicity of silica were certain phenazines, complexes of aluminium chelating agents, and the histamine-releasing agent L 1935. The protection against silica, it was shown, can be dissociated from the histamine-releasing activity of these compounds.

It is proposed now to test the more important compounds in mice.
A. Meiklejohn

SCHLIPKÖTER, H. W., THEWS, W. & DOLGNER, R. Die Quartz-Agglutinations-Reaktion mit dem Serum Silikose-Kranker. **[Quartz-Agglutination Reaction with the Serum of Patients with Silicosis]** *Deut. med. Woch.* 1959, May 15, v. 84, No. 20, 939–41, 955, 971, 2 figs. on pl.

In this paper some account of published work on the quartz-agglutination reaction precedes a description of the technique and results of tests of this reaction carried out by the authors on the sera of 73 patients with silicosis, 12 who had uncertain silicosis, 42 miners in whom though they had been exposed to silica dust no X-ray or clinical evidence of silicosis was found and 63 controls who had no history of dust exposure.

The results of the tests are described with a numerical table and a photograph of a positive and a negative reaction. No correlation between the test findings and the presence of silicosis was established. In the silicosis group of 73 persons 26 gave a positive and 47 a negative reaction, and in the control group of 63 persons the results were positive in 39 and negative in 24.
M. E. Delafield

GAULTIER, M., GUYOTJEANNIN, C. & FOURNIER, E. Recherche de la protéine C-Réactive dans le sérum de sujets atteints de silicose pulmonaire. **[Investigations of the Serum of Silicotic Subjects for the Presence of C-Reactive Protein]** *Arch. Malad. Professionnelles.* Paris. 1959, Jan.–Feb., v. 20, No. 1, 90–94. [Refs in footnotes.]

After reviewing the many pathological conditions associated with the presence of C-reactive protein in the serum, the authors expected that this protein would also be found in the serum of silicotic subjects; they therefore examined 40. Full details of the technique used are given. A positive result was obtained in 12, one of whom had superadded pulmonary tuberculosis. The test is simple to perform and is considered particularly useful in the those patients who are being treated with cortisone.
D. Rivers

GUYOTJEANNIN, C. & GUYOTJEANNIN, N. L'hypercoagubilité du sang dans la silicose. **[Increase of Coagulability of the Blood in Silicosis]** (2e note.) *Arch. Malad. Professionnelles.* Paris. 1958, Jan.–Feb., v. 19, No. 1, 67–71.

The mean coagulation time of the blood of 22 patients with silicosis was estimated to be 33½ minutes, which was significantly less than that found for a batch of normal controls. With a test developed by SOULIER and LE BOLLOCH the coagulation times of these blood samples, after addition of standard amounts of heparin, were found to be shorter than those of normal controls. Further study of blood coagulation in cases of silicosis is in progress.
D. Rivers

GAULTIER, M., GUYOTJEANNIN, C. & FOURNIER, E. Étude de la cuprémie chez les silicotiques. **[Study of Serum Copper Levels in Silicosis]** *Arch. Malad. Professionnelles.* Paris. 1958, Nov.–Dec., v. 19, No. 6, 592–5.

Serum copper was estimated in 40 cases of silicosis of various grades, 4 of which were complicated by pulmonary tuberculosis. The values for serum copper varied from 100 μgm. to 295 μgm. (mean value, 181 μgm.; standard error, 47·8 μgm.). Serum copper was raised in 27 of the patients, normal in 7, and subnormal in 6. Repeat estimates were made in 6 of the patients after an interval of 5 months. There was good agreement of the 2 separate estimates for each case. The ESR (Westergren) was estimated in 18 but the results were not found to be related to the serum copper levels. Raised serum copper levels in silicosis are considered to be in accord with the high copper and zinc contents found in the liquid obtained from ischaemic cavities in progressive massive fibrosis of coalworkers. CLAEYS and QUINOT have reported the presence of melanins in such fluid, and metallic enzymes are known to be important in the synthesis of such pigments. It is suggested that quartz may combine with proteins and the resulting cupro-proteins may be relevant to the association of tuberculosis and silicosis. Study of serum cupro-protein levels would therefore be useful. [The authors' speculations are not supported by their own results since of their 4 tuberculous cases 3 had serum copper levels well below normal values.]
D. Rivers

POWELL, D. E. B. & GOUGH, J. **The Effect on Experimental Silicosis of Hypersensitivity induced by Horse Serum.** *Brit. J. Exper. Path.* 1959, Feb., v. 40, No. 1, 40–43, 12 figs. on 2 pls. [17 refs.]

Rabbits were given quartz dust (0·5 to 1μ) intratracheally and then horse serum 7 days later. Hypersensitivity was maintained by further injections of serum at various intervals. There were 2 deaths from anaphylaxis. The sera of all these animals gave positive precipitin reactions with horse serum. Control animals received the same dose of quartz dust intratracheally. Test and control animals were killed at intervals up to 110 days after quartz injection. In the hypersensitive animals the silicotic lesions in the lung became larger and more discrete earlier, collagen matured earlier, and the quartz particles were more compact in the foci. No lung lesions attributable to horse serum were observed. The effects of the horse serum are considered to be the reverse of those due to cortisone. [The differences are possibly quantitative and not qualitative and may therefore not be relevant to the antigen-antibody hypothesis of silicosis or to Caplan's syndrome.] *D. Rivers*

VIGLIANI, E. La réparation de la silicose. [**Compensation for Silicosis**] *Arch. Malad. Professionnelles.* Paris. 1958, Sept.–Oct., v. 19, No. 5, 521–8.

The author reviews the more common problems encountered in assessing compensation for silicosis and describes briefly the different criteria which have been adopted by the 6 member countries of the European Community. The necessity for standardizing radiographic technique, diagnostic criteria, tests of pulmonary function and assessment of capacity for work is stressed. Of special importance in compensation assessment is the difficulty in deciding whether chronic bronchitis and emphysema is related or unrelated to the silicosis in a particular case. Research should be directed as rapidly as possible to reduce the errors both of diagnosis and of assessment of disability. *D. Rivers*

BARBERÁ ARMELLES, V. Silicosis en fundición. [**Silicosis in Foundries**] *Med. y Seguridad del Trabajo.* Madrid. 1958, July–Sept., v. 6, No. 24, 13–24, 2 figs. English summary.

This paper is based on a study of 20 cases among 1,061 workmen. Silica is contained in the ingredients of the mould employed: the sand or gravel used is selected for its porous and plastic qualities. A description is given of the composition of all the ingredients used in the foundry studied together with the results of analysing their chemical and physical structure and, where appropriate, the size of the silica particles. Some of the samples of sand contained up to 98% of silica. In addition to sand and clay the mixture comprising the mould contains horse dung, animal hair and powdered charcoal. Certain processes require the use of gums and starches, graphite and iron oxide.

There is a technical account of the 9 different kinds of mould actually used at the foundry and of the temperatures to which they are subjected: 1,550–1,580°C. for steel castings; 1,400°C. for iron and 1,000–1,100°C. for bronze.

The ideal preventive measure would be to find a suitable matrix for the moulds which does not contain silica but this has not yet been found though experimental work is being done in Sweden. The next best is to control the dust. This is helped by sending it up high and large chimneys. Attention must, also, be paid to the preparation and transportation of the matrix within the foundry. The raw materials should be received in a special building well removed from the places where the workmen congregate and with doors and windows on every side so that they can be opened or closed depending on the direction of the wind.

Transport from the storage building to the mixing mill should be on a moving belt running through a tunnel or surrounded by a metal cover. Water should be added just before the material reaches the foundry. If the matrix is needed at many points protected mechanical vehicles filled by means of a chute can be used.

The workers exposed to the greatest danger are those engaged in cleaning the casts after moulding. The casts are put on a vibrating metallic grid and the heavier parts of the mould break off and fall through. A strong downward current of air helps in this process and the cast is then lifted into a closed chamber where it is sprayed with water under considerable pressure. The final process is to remove grains of sand, vitrified by the violent temperature changes, by means of granulated steel in rotating drums but for very large casts jets of sand are used.

The employees should have periodic routine examinations of their chests and if any sign of lung disease should be discovered the man's work should be changed. The use of broncho-dilator aerosols is mentioned as helpful. *Allen Daley*

CALDWELL, D. M. **The Coalescent Lesion of Diatomaceous Earth Pneumoconiosis.** *Amer. Rev. Tuberculosis.* 1958, Apr., v. 77, No. 4, 644–61, 13 figs.

The author reports observations, over a period of 10 years, on 8 subjects who had worked in the diatomaceous earth industry. 4 patients had proved active tuberculosis, of whom 3 came to autopsy and from the other the right lung was removed surgically. All the specimens showed diatomaceous earth pneumoconiosis and fibrocaseous tuberculosis. In 2 other patients the radiological appearances were similar to the previous 4 patients but no tubercle bacilli could be isolated from sputum despite careful search. Tuberculin tests were positive. There was clinical and radiological improvement in both so that no lung pathology was available. In 2 further patients whose chest radiograph showed dense opacities the sputum and tuberculin tests were negative and it is considered that these cases were pure diatomaceous earth pneumoconiosis. Antibiotic therapy is recommended in all cases of diatomaceous earth pneumoconiosis with a positive tuberculin reaction and wider recognition of the early

radiological changes is regarded as important. [Larger photographs of the sections of lung and some representative photomicrographs would have helped one to appreciate the pathology.] *D. Rivers*

MITCHELL, J. **Pulmonary Fibrosis in an Aluminium Worker.** *Brit. J. Indust. Med.* 1959, Apr., v. 16, No. 2, 123–5, 3 figs.

No case of Shaver's disease [this *Bulletin*, 1949, v. 24, 662], aluminium pneumoconiosis, has hitherto been confirmed in Great Britain.

A youth aged 19 years, who had worked previously only as an agricultural labourer, started work in March 1951 at a factory where he was employed on a stamping machine in the production of fine aluminium powder. He was exposed to very high concentrations of this dust for about 4 hours each day. 3 years later he began to suffer from breathlessness, which rapidly became worse until he was totally disabled and confined to his bedroom. He died on 30 August, 1954. A few months before his death he was admitted to hospital for investigation. He was found to be suffering from diffuse fibrosis of the lungs which after exclusion of tuberculosis, sarcoidosis, syphilis, malignant infiltration, lipoid pneumonia, the reticuloses and Hamman-Rich syndrome, was thought to be due to the inhalation of aluminium dust. At necropsy, with the exception of the heart and lungs, all the organs were healthy. The heart was enlarged (weight 16 oz.), mainly the right ventricle. The lungs showed general fibrosis and interstitial emphysema. Histologically the fibrosis was non-nodular. Chemical examination of lung tissue revealed heavy impregnation with aluminium dust.

The case is considered to be indistinguishable from Shaver's disease, although spontaneous pneumothorax did not occur. The author suggests that the pulmonary fibrosis was due to a susceptible subject inhaling high concentrations of fine aluminium dust.

[Individual susceptibility can hardly be relied on as an adequate explanation for, according to a footnote, 3 other cases, 1 fatal, have since been diagnosed at the same works. The article gives little detail of the processes or manufactures at this particular factory. The cases call for an urgent and intensive study of the dust and associated environmental conditions and the medical supervision of the workers.]

A. Meiklejohn

UEDA, M., MIZOI, Y., MAKI, Z., MAEDA, R. & TAKADA, R. **A Case of Aluminium Dust Lung. A Necropsy Report.** *Kobe J. Med. Sci.* 1958, June, v. 4, No. 2, 91–9, 6 figs. (3 coloured). [18 refs.]

This is a full case report of a man aged 32 years who died 3 years after giving up work in which he had been exposed to the inhalation of metallic aluminium dust for only 3½ years. The main necropsy findings were a chronic interstitial pneumonia with severe cavitation in the right upper lobe and numerous small cavities in the rest of both lungs. Miscroscopically, some black and brownish granules and pigments in phagocytes were present in the interstitial tissue. The presence of excess aluminium in the lungs was confirmed both by spectroscopic and quantitative chemical analysis. There was no excess of copper, iron or other minerals in the lungs. Analysis of the airborne dust in the factory showed it to contain 96% aluminium dust, of which 99·3% was metallic aluminium, and stearic acid 4%, with traces of silicon iron and copper. This is claimed to be the first case report of chronic lung disease due to aluminium dust in Japan.

D. Rivers

KING, E. J., HARRISON, C. V., MOHANTY, G. P. & YOGANATHAN, M. **The Effect of Aluminium and of Aluminium containing 5 per cent. of Quartz in the Lungs of Rats.** *J. Path. & Bact.* 1958, Apr., v. 75, No. 2, 429–34, 8 figs. on 2 pls. [16 refs.]

In view of reported cases of severe disease caused by fine metallic aluminium in Germany [this *Bulletin*, 1943, v. 18, 57, 393, 394, 651] and by mixed oxides of aluminium and silicon in Canada [*ibid.*, 1947, v. 22, 643], it seemed important to compare the effects of metallic aluminium dust (under 1μ) and of aluminium dust with 5% quartz (under 5μ). The dusts were suspended in saline and were administered intratracheally to rats. Full details of the experimental technique are given. Rats were killed at monthly intervals up to one year. In the rats injected with aluminium, focal deposits of dust, situated subpleurally, were easily recognizable at 60 days after injection, the foci were collagenous at 120 days, and more densely collagenous with confluent lesions at 210 days. Aurine staining showed that the metallic aluminium was gradually converted to the hydroxide. In the lungs of the rats which had received aluminium containing 5% quartz there was already evidence of confluence of foci at 150 days after injection. A few confluent lesions were also present at 60 days. The entire base of the lung was fibrotic, shrunken and hard at 180 days. There was massive fibrosis at the end of one year. Most animals showed dilatation of bronchi and other bronchiectatic changes after 240 days. The lymph nodes were also much enlarged and fibrosed. On the whole there was slightly more fibrosis in the lungs of the rats which received aluminium plus 5% quartz than in those which received aluminium dust alone.

D. Rivers

ENGELBRECHT, F. M., BYERS, P. D., STACY, B. D., HARRISON, C. V. & KING, E. J. **Tissue Reactions to injected Aluminium and Alumina in the Lungs and Livers of Mice, Rats, Guinea-Pigs and Rabbits.** *J. Path. & Bact.* 1959, Apr., v. 77, No. 2, 407–16, 10 figs. on 3 pls. [29 refs.]

Most experiments particularly with rabbits and guineapigs appear to indicate that aluminium and alumina are not fibrogenic. On the other hand some workers, including King *et al.* [this *Bulletin*, 1955, v. 30, 1082] have produced massive fibrosis in rat lung with large amounts of intratracheal hydrated alumina and less but definite fibrosis both with the alumina fume from a corundum furnace and with aluminium phosphate. This conflict of experience conforms to

observations among workmen exposed to heavy concentrations of aluminium and alumina dusts in the course of employment. These various experiences suggest that there may be a species difference in the tissue reactions to aluminium and alumina.

Metallic aluminium powder and hydrated alumina powder were injected into the lungs of rabbits. Only a mild degree of fibrosis was produced. In a second experiment the hydrated alumina was injected intratracheally into rats, mice, guineapigs and rabbits, and intravenously into mice, guineapigs and rabbits. The rats developed numerous nodules of dense fibrosis. Mice and guineapigs developed a reticulin network with occasional collagen fibres, while rabbits showed only a slight reticulin network. The reaction of the liver of mice, guineapigs and rabbits to intravenously injected alumina was minimal. There thus appears to be a marked species difference to the fibrogenic action of alumina.

A. Meiklejohn

STACY, B. D., KING, E. J., HARRISON, C. V., NAGELSCHMIDT, G. & NELSON, S. **Tissue Changes in Rats' Lungs caused by Hydroxides, Oxides and Phosphates of Aluminium and Iron.** *J. Path. & Bact.* 1959, Apr., v. 77, No. 2, 417–26, 11 figs. (10 on 4 pls.)

Aluminium and certain relatively insoluble aluminium compounds, the hydroxide γ AlOOH and the phosphate berlinite ($AlPO_4$ with a crystal structure similar to quartz) were shown by King and his co-workers [this *Bulletin*, 1955, v. 30, 1082; see also above] to behave as fibrogenic materials when injected into the lungs of rats. As aurine-stained sections did not reveal free aluminia it was suggested that aluminium-protein complexes might be the cause of the fibrosis. These observations came as a surprise, because previously silica was believed to be unique in having specific fibrogenic properties. It was therefore considered advisable to extend the range of observations.

In parallel studies in experimental silicosis it was found that size and crystal structure of silica influenced fibrogenic activity in rats' lungs. In particular, tridymite acted more strongly than quartz. As aluminium phosphate exists in the same modifications as silica it was decided to test a number of aluminium oxides or hydroxides and to extend the study also to the phosphate and hydroxides of iron.

The characteristics of aluminium and iron hydroxides, oxides and phosphates used for the injections were as set out below.

The solubilities of the aluminium compounds were determined at room temperature after 3, 6, 22, 38 and 73 days. Dust suspensions were prepared so that the required dose was contained in 1 ml. of normal saline. Groups of 12 or 15 rats were injected intratracheally and the animals were killed at monthly intervals over a period of 1 year. The resultant fibrosis of the lungs was graded histologically according to scale of BELT and KING [*ibid.*, 1945, v. 20, 776]:

grade 1, loose reticulin and no collagen; grade 2, compact reticulin with or without a little collagen; grade 3, somewhat cellular but made up mostly of collagen; grade 4, wholly composed of collagen fibres and virtually acellular; grade 5, acellular, collagenous, confluent.

γ-Al_2O_3 was found to be the most fibrogenic material, reaching grade 3 after 3 months and grade 4 or 5 after 7 months. Next in order of fibrogenicity were the quartz-like and tridymite-like modifications of $AlPO_4$ but whereas in corresponding experiments with silica, tridymite had been found to be more fibrogenic than quartz, the two varieties of $AlPO_4$ acted equally. α-Al_2O_3 was almost inert, and all iron compounds tested were completely so.

There was a positive correlation for the aluminium oxides and hydroxides between alumina solubility and fibrogenic activity, but the alumina phosphates were more fibrogenic than their solubility suggested.

A. Meiklejohn

Material	X-no.	Degree of crystallinity	Mean particle diameter (μ)*	Dosage (mgm./rat)	No. of rats
Aluminium hydroxides and oxides					
γ-AlOOH,HX10l0	1046	poor	c.0·02	(70+	12
				(14	12
γ-AlOOH, Cera hydrate	823	good	3	60+	12
γ-Al_2O_3,HX10l0 at 850°C.	1342	poor	c.0·02	50	12
α-Al_2O_3,HX10l0 at 1200°C.	1336	good	<1	50	12
Iron hydroxides					
α-FeOOH	1418	medium	<1	100	15
γ-FeOOH	1370	medium	<1	100	15
Aluminium phosphates					
$AlPO_4$, quartz structure	2518	good	2	50	15
$AlPO_4$, tridymite structure	2507	good	2	50	15
Iron phosphate					
$FePO_4$, quartz structure	2267	good	2	100	15

*assessed from electron photomicrographs.
+ equivalent to 50 mgm. Al_2O_3.

LEATHART, G. L. **The Mechanical Properties of the Lung in Pneumoconiosis of Coal-Miners.** *Brit. J. Indust. Med.* 1959, Apr., v. 16, No. 2, 153–65, 7 figs. [31 refs.]

"To assess changes in the mechanical properties of the lungs in pneumoconiosis, the 'elastance' (coefficient of elastic resistance, the reciprocal of compliance) of the lung and resistance of the airways were measured by the method of Mead and Whittenberger (1953) in 97 coal-miners and 17 men who had never worked underground. Ages ranged from 24 to 57. The work done on the lung was measured in 66 of these subjects, and the maximum voluntary ventilation (M.V.V.) was measured in all. The subjects were obtained by random selection from hospital out-patients and by random selection from a radiological survey of over 5,000 coal-miners. The M.V.V. was reduced in coal-miners with progressive massive fibrosis (P.M.F.), and in those without pneumoconiosis, but was not significantly reduced in simple pneumoconiosis. Elastance of the lung was unaltered in young miners but was slightly, and significantly, increased in all elderly faceworkers whatever the radiological category. This change appeared to be due to long years of work underground rather than to the radiological abnormality of pneumoconiosis. This slight change in the pulmonary elastance cannot be the cause of the reduction in M.V.V., since the two are unrelated. Inspiratory resistance was normal in all coal-miners, suggesting that pneumoconiosis is not associated with any fixed distortion of the airways. The non-elastic work of breathing, however, was frequently above normal and this suggests that bronchial obstruction develops rather commonly during expiration. This change appears to be the cause of reduction of M.V.V. in the majority of cases, as a negative correlation between M.V.V. and non-elastic work was established. Mean non-elastic work was not, however, unduly high in those radiological groups in which a significant reduction of M.V.V. was recorded. It is suggested that this discrepancy may be due to excessive frictional resistance in the chest wall of miners with P.M.F. and those with no radiological abnormality. The findings are consistent with the hypothesis that emphysema is abnormally common in elderly coal-miners, and that it, rather than pneumoconiosis, is the cause of their reduced ventilatory ability."

LONI, N., BELLOIU, D., SĂHLEANU, V. & HOLBAN, R. Studiu experimental asupra modificărilor hematologice si endocrine în abataje. [**An Experimental Study on Haematologic and Endocrine Changes in Animals kept in Coal-Pits**] *Igiena.* Bucharest. 1959, Jan.–Mar., v. 8, No. 1, 11–20, 14 figs.

The English summary appended to the paper is as follows:—

"Guinea-pigs kept for 4 months in the galleries of coal-pits displayed anthracotic and pneumokoniotic lesions in the lungs as well as marked anaemia. The endocrine changes differed according to environmental temperature and consisted in adrenal and thyroid stimulation in cold galleries and in thyroid inactivation with testicular lesions in the hot galleries. The regeneration of red blood cells was insignificant in hot galleries and very marked in cold galleries. To a certain extent these differences might be related to the functional state of the endocrine glands, and particularly of the thyroid. The percentage decrease of eosinophiles, which was more intense in the cold gallery, may be interpreted as a haematologic response to adrenocortical stimulation.

"A classification is outlined of the various ways in which the endocrine system is influenced by labour conditions and harmful occupational agents."

LOUVAIN: Union des Ingenieurs sortis des Ecoles Speciales de l'Université Catholique. Journée d'Etude consacrée à l'Hygiène des Mines. [**Association of Engineers from Special Departments of the Catholic University of Louvain Study Day in Mining Hygiene**] 3. 5. 1958. 166 pp., numerous figs. [Numerous refs.] [1959.] Brussels: 66, av. de la Toison d'Or.

R. MERCIER, President of the Association, opened the proceedings before a distinguished audience which included the Belgian Minister of Mines, members of the government and representatives from other associations. He underlined that in recent years mining engineers in the Belgian coal-mines had faced an increasing responsibility for the control of industrial accidents and diseases. As evidence of their activities in this field he recalled the recent study days organized by the mining groups of Mons and Liège.

A. SOILLE, Chairman, in outlining the programme described the tremendous problems of health and ventilation, which had followed the introduction of mechanization in coal-mines.

The programme comprised 12 papers by members of the local association and visitors.

The following list of contributions gives a good idea of their nature and range. The articles have been printed in full but without record of any discussions.

It would appear that the official languages of the conference were Flemish and French and for those wishing to consult the texts there is the difficulty that some are in French with an abstract in Flemish (papers 2, 6, 8 and 10) and the others *vice versa.*

F. LAVENNE. Problèmes posés par le développement de la pneumoconiose des houilleurs. Leur importance au point de vue de la prévention [Problems arising from Coalworkers' Pneumoconiosis and their Significance in Relation to Prevention]. pp. 11–27, 89 refs.

V. VAN MECHELEN. Diagnostic, classification et évolution de la pneumoconiose des houilleurs [Diagnosis, Classification and Course of Coalworkers' Pneumoconiosis]. pp. 28–36.

G. DEGUELDRE. Techniques de prélèvement, examen et analyse des poussières [Sampling Techniques and Examination and Analysis of Dusts]. pp. 37–55, 42 refs.

F. Rey. Les mesures d'empoussiérage dans les houillères françaises et l'état actuel des procédés techniques de lutte contre les poussières [Dust Measurements in Coal-mines in France and Technical Measures for Control of Dust]. pp. 56–62.

M. Alexis. La lutte contre les poussières en taille [The Control of Dust at the Coalface]. pp. 63–73.

J. Delhaye. Mécanisation et hygiène [The Influence of Mechanization on Hygiene in Coal-mines]. pp. 74–81.

H. Lavallee. État actuel de la lutte contre les poussières en taille aux Charbonnages de Houthalen [The State of Dust Control at coalface in the collieries at Houthalen]. pp. 83–94, 12 refs.

A. Minette. État actuel de thérapeutique pulmonaire chez les houilleurs [The Current State of Treatment of Pulmonary Disease in Coal-miners]. pp. 95–104, 59 refs.

A. Houberechts. Le climat souterrain et la réfrigération de l'air de ventilation des mines [The Underground Climate and Cooling of Incoming Air in Mines]. pp. 105–36, 67 refs.

W. De Braaf. Rapport entre ventilation et hygiène [Relationship of Ventilation to Hygiene of Mines]. pp. 137–44, 10 refs.

O. De Crombrugghe and J. Patigny. Ventilation minière. Méthodes récentes pour l'étude de réseaux maillés [Mining Ventilation. Recent Methods in the Study of Intersections]. pp. 145–62, 29 refs.

E. Massacesi. Le rôle de la C.E.C.A. dans les recherches du domaine de l'hygiène des mines [Role of the Association of Coal and Steel Industries in the Field of Mining Hygiene]. pp. 163–6.

[The 3 medical papers constitute an excellent survey of current knowledge of coalworkers' pneumoconiosis throughout the world. Among the main topics discussed are simple and complicated pneumoconiosis with special reference to the role of tuberculous infection in the pathogenesis of the disease.

The mining papers review current methods of dust collection and analysis and methods of dust control at the coalface and elsewhere underground. The various methods of water infusion are specially discussed. Dust is not the only problem; ventilation and temperature control are no less important.

It is apparent that mining engineers in Western Europe regard the health problems of coal-miners as a challenge. Not only is each of the groups making a great effort to meet the challenge locally but by such study days as the above they are coordinating their efforts by sharing knowledge and experience.]

A. Meiklejohn

Seeler, A. O., Gryboski, J. S. & MacMahon, H. E. **Talc Pneumoconiosis.** *Arch. Indust. Health.* Chicago. 1959, Apr., v. 19, No. 4, 392–402, 13 figs. [11 refs.]

Pure talc is hydrous magnesium silicate [Hg_2 Mg_3 $(SiO_3)_4$] but talc used in industry varies widely in composition according to its place of origin. Thus some samples have been found to contain up to 40% free silica and these under suitable conditions may cause silicosis. Cases of talcosis have been reported from several countries but very few have included post-mortem observations.

2 workmen, who for 22 and 30 years respectively had been exposed to high concentrations of talc dust, died. For many years both had suffered from chronic pulmonary disease, which was characterized clinically by considerable impairment of vital capacity and pulmonary ventilation and radiographically by diffuse fibrosis of the lungs with bullous emphysema. Their work at a cable works involved the constant shovelling of talc on to layers of rubber. All the talc came from the same mine; particle size varied from 1μ to 150μ, 90% being under 10μ. Analysis of the talc below 10μ in size showed 8% talc, 68% dolomite, 3% magnetite, 16% serpentine and 5% other minerals; the free silica content was less than 0·5%. At necropsy the gross and microscopic findings included extensive fibrosis of the lungs, dilatation of bronchi and alveoli and damage and destruction of blood vessels. Histologically there was no evidence of whorled nodules of silicosis. Large quantities of doubly refractile material, which on examination by X-ray diffraction consisted of needle-like particles of talc, were present throughout the lung tissue. Talc, it is concluded, must be regarded as a material capable of causing pneumoconiosis; the fibrosis is a non-specific reaction to talc spicules. [The article is well illustrated by X-ray photographs and photomicrographs of lung tissue.]

A. Meiklejohn

Chabot, B., Froeb, H., Pivoteau, C. & Sadoul, P. Étude de la ventilation alvéolaire par la mesure du CO_2 artériel et du CO_2 expiré. Conditions de mesures. Valeurs normales. [**Evaluation of the Alveolar Ventilation by the Measurement of Arterial CO_2 Output. Conditions Necessary for the Evaluation. Normal Values**] Reprinted from *Rev. Méd. Nancy.* 1957, July, v. 82, 695–706, 2 figs. [17 refs.]

With the Fleisch metabograph alveolar ventilation was assessed in 10 normal human beings from volume of expired CO_2 divided by alveolar CO_2 concentration, and from this the physiological dead space was derived from difference between total and alveolar ventilation divided by respiratory rate. Alveolar CO_2 concentration was derived from its known close approximation to arterial CO_2 concentration obtained by arterial puncture. The reproducibility of the primary measurements and causes of inaccuracy are discussed at length.

M. L. Thomson

SADOUL, P., CHABOT, B. & PILLOT, P. Considérations sur la ventilation alvéolaire des insuffisants respiratoires. [**Consideration of the Alveolar Ventilation in Respiratory Insufficiency**] Reprinted from *Rev. Méd. Nancy*. 1957, July, v. 82, 707–23, 8 figs. [10 refs.]

With the above techniques 126 studies have been carried out on 102 patients with respiratory insufficiency, which included pulmonary tuberculosis (39), emphysema (23), pneumoconioses (18), bronchial asthma (10), bronchiectasis (5) and bronchial carcinoma (3).

One group had a lower than normal alveolar CO_2 tension, alveolar ventilation greater than 3 litres per square metre per minute and manifest hyperventilation. In most of these patients this was due to stress of the examination. Where CO_2 tension and alveolar ventilation are within normal limits it cannot be concluded that ventilatory insufficiency is not present; these values may be maintained only at the cost of increased total ventilation. Where alveolar ventilation, although approaching the normal value of 2·5 litres per square metre, does not maintain normal CO_2 tension, the defect must be impaired ventilation or failure of respiratory regulation.

The timed vital capacity test has been found useful in selecting patients in whom these tests are likely to be particularly useful. *M. L. Thomson*

SZEWCZYKOWSKI, W. Symptomatologia wczesnej ołowicy i wartośc badań laboratoryjnych w jej rozpoznawaniu. [**Semeiology of Early Lead Poisoning and the Value of Laboratory Tests for its Diagnosis**] *Ann. Univ. Mariae Curie-Skłodowska*. Lublin. Sect. D. 1957, v. 12, 173–217. [29 refs.] English summary.

In an examination of 35 workmen exposed to lead poisoning for 1–40 years 14 were found to suffer from general weakness, 10 from headaches and 10 from abdominal pains; a lead line was present in 18, anaemia in 11 and hypertension in 4; the results of clinical investigation are given in detail in tables. Only 2 persons showed none of the signs of lead poisoning. A similar investigation was carried out on 63 workmen engaged in applying a lead glaze to tiles. Lead contents up to 2·075 mgm. per cubic metre were observed in the air of the working places; porphyrinuria was present in 27 and a lead line in 10 persons, 1 or more signs of lead poisoning being found in 45 persons (72%). The clinical findings are described in detail.
D. J. Bauer

LEWIS, C. E. **The Biological Actions of Vanadium. I. Effects upon Serum Cholesterol Levels in Man.** *Arch. Indust. Health*. Chicago. 1959, Apr., v. 19, No. 4, 419–25, 1 fig. [35 refs.]

24 men over the age of 40, exposed in their work to vanadium (V) for at least 6 months and not to other chemicals, were selected for investigation to find out whether V lowered serum cholesterol. Variables—age, alcohol, fat, race, height, etc., were controlled or shown by statistics not to be significantly related to the cholesterol values observed. 13 worked in Colorado, at 6,000 ft. above sea level, and 19 at Ohio, at 600 ft. 22 and 23 controls were selected by random methods from 68 and 60 volunteers in the specified age and physical activity ranges in the 2 places to reduce the geographical factor which was shown to affect the haematocrit, though not the cholesterol, values; there was no effect on the haematocrit from V alone. Examination involved a standardized medical and occupational history, a subjective evaluation of alcohol and fat intake, complete clinical examination, urinalysis, electrocardiogram and total cholesterol in serum from fasting subjects. It was important to exclude nephrosis, diabetes and thyroid dysfunction.

Urinary V excretion tests in 77 men ranged from 6 to 160 μgm per litre, and this brought to notice that in the original group were 8 exposed supervisors working in relatively uncontaminated areas for most of the time; their urinary values ranged from 7 to 11 μgm. per litre, they had none of the symptoms of other V workers and they were excluded from the exposed group. The mean urinary V concentration in 24 exposed men was 46 μgm. per litre and in 45 controls 12 μgm. Atmospheric concentrations of V (asV_2O_5) ranged from 0·018 mgm. per m^3 in the foreman's office to 0·925 mgm. per m^3 in the V_2O_5 dumping area, with intermediate values near furnaces, drying, precipitation and production areas; particles of less than 5μ accounted for 5–10%. The electrocardiogram was essentially normal in 37 controls and 20 exposed.

The mean concentration of cholesterol in the serum of the exposed group, 205 mgm. per 100 ml., was significantly lower than in that of the control group, 228 mgm. per 100 ml. *M. Patricia Fitzsimons*

WEMBER, G. Theoreticshe Betrachtung zu den Strömungsverhältnissen über einer Absauganlage, die nach dem Luftschleierverfahren arbeitet. [**Theory of the Air Flow Pattern above an Exhaust Slot Operating on Air Screening Process** (*Luftschleierverfahren*)] *Staub*. Düsseldorf. 1959, Apr. 1, v. 19, No. 4, 106–8, 4 figs.

The English summary appended to the paper is as follows:—

"The system of removing unhealthy vapours from above acid baths alone by the means of edge exhaustion is imperfect and uneconomical. The rising vapours cannot be effectively suppressed unless a layer of air is injected from one of the long sides of the bath across its surface in the direction of the exhaust duct mounted on the opposite side. This flow action is well illustrated by the determination of the flow pattern, the course of which is decisive for the forming of an, from the point of view of flow, advantageous shape of the exhauster slit. By way of considering analogies, it is possible to compute or calculate baths of other dimensions."

GERARDE, H. W. **Toxicological Studies on Hydrocarbons. III. The Biochemorphology of the Phenylalkanes and Phenylalkenes.** *Arch. Indust. Health*. Chicago. 1959, Apr., v. 19, No. 4, 403–18, 17 figs. [11 refs.]

This illustrated report on 32 alkyl derivatives of benzene ends with the suggestion that in toxicology

" phenylalkanes " is a better term for the alkylbenzenes because, unlike benzene, they have no myelotoxic effect. They are sparingly soluble in water, solubility and volatility decreasing with the number and length of the alkyl group. They accumulate in tissues with a high lipid content. Some are excreted unchanged through the lung, others as biotransformation products. Oxidative changes may take place at the beta, omega or penultimate carbons, and the metabolites after conjugation are excreted in the urine. Alkylbenzenes irritate skin, mucous membranes and endothelium. Pulmonary haemorrhage or pneumonitis, with contributory respiratory failure, was the principal cause of death following oral or parenteral administration. All organs were hyperaemic or haemorrhagic. The spleen and thymus were not involuted. On the central nervous system they have a temporary, physical depressant effect; its duration increases with the length and branching of the side-chain. The narcotic potency decreases with chain length. Branching and unsaturation increase the irritant effect; lengthening and multiplicity decrease it. Alkylation affects odour and taste, *e.g.* thymol, menthol and eucalyptus, but phenyldodecane is bland and oily with the narcotic potency of mineral oil.

Mortality ratios, for groups of 10 rats, weighing 250 gm., given 1 oral dose of 2·5 ml. of a mixture of the hydrocarbon in olive oil, 1 : 1 v/v, show for example: branched-chain monoalkylbenzenes (isopropyl, 6/10, *sec*-butyl, 8/10, *tert*-butyl, 7/10, *sec*-amyl, 9/10 and *tert*-amyl, 5/10) were more toxic than the corresponding straight-chain isomers with ratios of 2/10; dialkylbenzenes containing 2 irritating branched alkyl groups (di-isopropyl, *p*-di-*tert*-butyl and di-*sec*-amyl) gave ratios of 0/10.

Threshold limits range from 10 p.p.m. for *p-tert*-butyltoluene to 200 p.p.m. for toluene and the xylenes, based on mucous membrane irritation rather than systemic toxicity. Stromatolysis was demonstrated with benzene, toluene, *o*-xylene, phenylacetylene and indene, and with indene it was also demonstrated *in vivo* in the lung.

[See also this *Bulletin*, 1956, v. 31, 1022.]

M. Patricia Fitzsimons

MAGOS, L., BÁTSKOR, Ilona & CSENKEY, L. Szénkénegártalom a müselyemgyártással kapcsolatban. [**Carbon Disulphide Poisoning in Artificial Silk Manufacture**] *Egészségtudomány*. Budapest. 1958, v. 2, No. 3, 228–37. [37 refs.] German summary.

An investigation has been made of the effects of exposure to carbon disulphide on workers in an artificial silk factory. Mean air concentrations as high as 2,933 mgm. per cubic metre were observed in certain working situations, together with mean concentrations of hydrogen sulphide up to 32·6 mgm. per cubic metre. Conjunctivitis was frequently encountered, with 207 cases in 1955 with a loss of 396 working days. Determination of the concentration of carbon disulphide in the blood was carried out on 35 workers who had been exposed for 2 years; concentrations of 41–80 μgm. per litre were found in 11, and of 201–500 μgm. per litre in 6 instances; 20 complained of headaches and 12 of anorexia. On neurological examination only 8 workers showed no signs of nervous involvement; the remainder suffered from cerebral vascular disorders of varying extent and 10 from hypertension. *D. J. Bauer*

GRAY, E.LeB. **Oxides of Nitrogen: Their Occurrence, Toxicity, Hazard. A Brief Review.** *Arch. Indust. Health*. Chicago. 1959, May, v. 19, No. 5, 479–86. [51 refs.]

YAMADA, Y. **Studies on the Experimental Chronic Poisoning of Nitrobenzene.** *Kobe J. Med. Sci.* 1958, Dec., v. 4, No. 4, 27–39, 10 figs. [55 refs.]

Detoxification mechanisms and the course of poisoning were assessed each week by several biochemical estimations and full blood counts in rabbits subcutaneously injected with 0·7 ml. per kgm. of nitrobenzene daily, the maximum dose found by preliminary experiments not to cause death from acute poisoning. Serial results are given for 8 rabbits. 3 died in the 4th week, 2 in the 6th, 1 in the 11th, 1 in the 14th and the last was killed in the 24th.

Judging from the course of the anaemia, and also from the amounts of detoxification products in the urine which indicated when amination, acetylation and hydroxylation were intense or weak, the process could be divided into 3 characteristic stages. During the initial response stage there was a pronounced reaction to the poison, shown by early and progressive anaemia and an increased and fluctuating urine content of NO_2, NH_2, total- and ethereal-glucuronic acid and sulphuric acid, with aggravation of general symptoms, loss of appetite and weight, towards the 5th week. The second, the resistance stage, lasted about 10 weeks during which there was recovery from anaemia and continuous high excretion with little fluctuation of detoxification products, hydroxylation being more intense. Towards the 15th week anaemia recurred, excretion levels diminished and the animals, until then healthy in appearance, became emaciated before death in the third, the exhaustion stage. In extent and degree of pathological findings there was little difference between the animals which died early and those poisoned for 3–5 times longer, except in the adrenal cortex. In those dying early adrenal hypofunction was deduced from regressive degeneration and lack of fatty granules in the fascicular layer. In the others there was little or no cortical degeneration, suggesting superior resistance, but whether congenital or acquired was not yet clear.

M. Patricia Fitzsimons

MACCHERINI, I. & CAMARRI, E. L'intossicazione da nitroderivati dei glicoli. [**Nitroglycol Poisoning**] *Med. d. Lavoro*. 1959, Mar., v. 50, No. 3, 193–201. [30 refs.] English summary (7 lines).

The authors describe occupational disease in persons working with anti-freeze dynamite which in addition to nitroglycerin contains di-nitroglycol, and nitroglycol for their properties of lowering the freezing-point of nitroglycerin. Knowledge of the action of nitroglycol in man is slight. Owing to its high volatility absorption is mostly by inhalation, though it can also be absorbed through the skin.

Symptoms start when work is begun and consist essentially in vasomotor phenomena which usually disappear within 2 to 3 weeks, but the most typical manifestations are stated to be anginoid crises occurring about 48–60 hours after finishing work.

187 men and 78 women working with anti-freeze dynamite and 25 controls, who although working in the same factory had neither direct nor indirect contact with the substance, were examined both clinically, and by a battery of laboratory and ancillary tests, both during working hours and where possible on rest days also.

All the operatives were aged between 25 and 60 years, mostly 35–50. Almost all complained of some upset after beginning work at the factory, the symptoms in both men and women being headache, palpitation, nausea, and a sensation of heat on the face and extremities; the symptoms which varied in intensity from case to case, gradually disappeared in a few weeks. Out of a group of 70 workers who had more opportunity of coming into contact with dynamite than the others, 10 had anginoid crises between 40 and 60 hours after leaving work, with constrictive precordial pain running up to the left side of the neck and down the left arm lasting for a few minutes but not recurring that day. These patients were aged from 40 to 50 years and had worked for between 8 and 15 years at the factory. The ECG was negative in all.

The clinical findings were almost entirely negative in all those examined except that out of 265 workers, 50% had hypotension, but only during working hours and more often in those working in the departments where there was direct contact with dynamite.

In a discussion of the mechanism of action the possibility is put forward of the anginoid crises arising through deficient O_2 consumption by the myocardium due to the inhaled nitro compounds causing dilation of the coronary arteries and an increased blood flow. After work ends there is an increased O_2 consumption by the myocardium not compensated for by increased coronary flow. The prolonged P-R interval found in a few cases in the ECG might be thus explained.

However the authors conclude that as present-day preventive methods have reduced the level of the volatile components below the toxicity level of 2mgm. per cu. metre, if care is taken to exclude from such work persons with hypotension, anaemia, or hyperthyroidism, little difficulty should arise. *W. K. Dunscombe*

MILLER, S. & EHRLICH, R. **Susceptibility to Respiratory Infections of Animals exposed to Ozone. I. Susceptibility to** *Klebsiella pneumoniae*. *J. Infect. Dis.* 1958, Sept.–Oct., v. 103, No. 2, 145–9.

Groups of Swiss white mice and golden hamsters were exposed to the following conditions: (a) different concentrations of ozone followed by aerosol infection with *Klebsiella pneumoniae* type A; (b) aerosol infection alone; and (c) ozone concentrations alone. There was also a control group of unexposed animals. In the ensuing 14 days the mortality rate and survival time of the groups were recorded. Exposure to ozone reduced the resistance of mice and hamsters to subsequent respiratory infection with *K. pneumoniae* as these animals showed higher mortality rates, shorter survival times, and a lower LD50 than the controls. The differences in the mortality rates and survival times were statistically significant. Post-mortem examination of surviving animals killed after 14 days showed that animals infected with *K. pneumoniae* had serous fluid in the pleural cavity and some oedema and haemorrhage of the lungs; animals with ozone exposure and infection with the bacterium had viscous purulent discharge surrounding the lungs, more oedema, and much more lung haemorrhage. Control animals and those exposed to ozone only showed no gross pathological changes. *Elizabeth M. Harper*

DALHAMN, T. Freon som orsak till förgiftningsfall. [**Freon as a Cause of Poisoning**] *Nordisk Hyg. Tidskr.* 1958, v. 39, Nos. 11/12, 165–9. English summary (5 lines).

Various types of Freon (chlorinated fluorinated hydrocarbons) are frequently used as ejecting gases in aerosol packs, and although they are not toxic they may nevertheless give rise to phosgene, hydrofluoric acid, hydrochloric acid, sulphur dioxide and chlorine in contact with hot surfaces in concentrations much higher than the maximum permissible levels. The possible occurrence of intoxication by Freon decomposition products was investigated by the author in a study of the records of cases of gas poisoning from all the hospitals in Sweden between 1950 and 1954. 43 cases occurred in all; 2 of these were due to phosgene poisoning, and brief histories are given. (1) a mechanic aged 52 operated with an acetylene torch upon a refrigerator which was discharging dichlorodifluoromethane (Freon-12) from a leak; he developed dyspnoea, malaise and vomiting, and required hospital treatment for 5 days. (2) An agricultural worker aged 47 sprayed his bedroom with an aerosol fly spray containing Freon, switched on an electric heater and then went to bed. He awoke in the night with malaise, vomiting and diarrhoea and died on the following day 3 hours after admission to hospital. *D. J. Bauer*

DAVIES, D. R. & GREEN A. L. **The Chemotherapy of Poisoning by Organophosphate Anticholinesterases.** *Brit. J. Indust. Med.* 1959, Apr., v. 16, No. 2. 128–34. [66 refs.]

Poisoning of mammals by the organophosphates that inhibit cholinesterase is believed to result from the accumulation of acetylcholine. Atropine which counteracts the action of acetylcholine at certain sites has long been recognized as an effective therapeutic agent in cases of poisoning by these compounds. Atropine only counteracts the effects of an inhibition of cholinesterase. This paper traces the development of work aimed at achieving a reversal of the inhibition with a reactivation of the enzyme. By studying the ability of certain groups, notably hydroxylamines, to react with alkyl phosphates and combining this group in a molecule containing a quaternary nitrogen, an effective reactivating

agent of low toxicity—pyridine-2-aldoxime methiodide (P_2AM)—was discovered simultaneously in 2 laboratories. The quaternary N is believed to attach itself to the enzyme at the same site as acetylcholine and so bring the oxime into close proximity to the alkyl phosphate group attached to the esteratic site on the enzyme. On reaction taking place the product leaves the enzyme. P_2AM especially if combined with atropine has been shown to be very valuable in poisoning by certain organophosphorus compounds.

Other compounds that react with organophosphates or reverse the inhibition are described but have various drawbacks including undesirable toxicity. Recently bisquaternary compounds resembling a double molecule of P_2AM have been shown to be more effective. The authors stress the important part played by fundamental biochemical studies in the development of these valuable therapeutic agents. *J. M. Barnes*

Golz, H. H. **Controlled Human Exposures to Malathion Aerosols.** *Arch. Indust. Health.* Chicago. 1959, May, v. 19, No. 5, 516–23, 4 figs.

16 prisoners volunteered for repeated exposures to nebulized spray material from standard aerosol cans containing malathion. Only 4 cases of poisoning by this widely used insecticide have been recorded and 3 of them were from ingestion. 3 sets of aerosol bombs were used. 1 set for the control group of 4 of the men, Group 1, contained only the basic propellant vehicle; another for Group 2 contained 5% malathion and the third for Groups 3 and 4 contained 20%, the malathion being substituted for identical amounts of Freon, the main constituent of the vehicle. Each group remained in their cell, 18 by 8 feet and 12 feet high, for 1 hour after the aerosol was sprayed above head level along the length twice daily on 7 days a week for 6 consecutive weeks. Each time Groups 1, 2 and 3 were exposed to between 5·1 and 5·6 gm. of the aerosol, an application rate of 3 gm. per 1,000 cu. feet, and Group 4 was exposed to 4 times this amount. The application rates of malathion for Groups 2, 3 and 4 were 0·15, 0·60 and 2·4 gm. per 1,000 cu. feet.

None of the subjects had cholinergic symptoms, though Group 4 experienced initial nasal and conjunctival irritation. Physical examinations were negative. Serial erythrocyte and plasma cholinesterase activities were determined from 2 weeks before until 1 week after the experiment. 18 results are presented for each man as a percentage of the mean of his 4 pre-exposure values. No cholinesterase activities fell below 90% of normal except in 2 subjects, though there were aberrant results among control and test subjects on 1 day due no doubt to technical error. Midway, the plasma cholinesterase values of 1 subject in Group 3 decreased steadily to 61%, and those of another in Group 4 fell to 83% and then fluctuated between 80% and 88%. However, there were no accompanying decreases in the erythrocyte cholinesterase activity, and the depressed plasma values were therefore probably not caused by the malathion.

M. Patricia Fitzsimons

Bourne, L. B., Milner, F. J. M. & Alberman, K. B. **Health Problems of Epoxy Resins and Amine-Curing Agents.** *Brit. J. Indust. Med.* 1959, Apr., v. 16, No. 2, 81–97, 18 figs. [24 refs.]

The authors discuss the chemistry of epoxy resins and of various curing agents; they give a review of toxic effects and of the incidence of dermatitis, experiments to find the cause for this, and a theory for the mechanism by which the highly reactive epoxy and polyamine groups associated with resin curing systems affect the skin; this survey shows the necessity for good engineering and for the stringent working precautions described. The cause of many cases of dermatitis appears to be uncombined amine which persists in hardened resins, particularly when cold-cured. Experiments are described which support this view. It appears desirable to replace amines by amides in those factories where no-touch techniques cannot be introduced.

M. Patricia Fitzsimons

Evans, D. M. **Two Cases of Hydrazine Hydrate Dermatitis without Systemic Intoxication.** *Brit. J. Indust. Med.* 1959, Apr., v. 16, No. 2, 126–7.

Hydrazine hydrate is a fuming liquid with a delayed irritant effect. Hydrazine intoxication may cause anorexia, loss of weight and, later, haemorrhagic pulmonary oedema and liver damage. 2 patients gave a history of having developed rashes after using hydrazine hydrate, having been in contact previously for 5 months at irregular intervals without rash. Neither showed signs of systemic intoxication. The picryl chloride colour reaction, modified to test for hydrazine on the fingers is described; it was positive in the patients and another man who had worked with hydrazine hydrate without developing dermatitis. In this man and the first patient the test was still positive the next day.

The MAC of hydrazine hydrate is 1 p.p.m. Gloves and goggles, lanoline on exposed skin and adequate ventilation are needed during contact. Eye irrigation bottles containing water and, when large quantities are used, a bath of tepid water should be convenient for rapid decontamination; breathing apparatus may be required. *M. Patricia Fitzsimons*

Young, W. C. & Monro, I. C. **Radioactive Contamination—The Wishaw Incident.** *Med. Officer.* 1959, May 15, v. 101, No. 20, 277–8.

3 small boys gave a lot of trouble to other people by poking about among the radio-active waste in a bin used by a firm using radio-active luminous paint. The Medical Officer of Health requested the chief constable to make a search for the boys; they were identified within 3 hours and on instruction from the police the boys were bathed and their clothing isolated. The next step was to take these tiresome boys up to the headquarters of the Radiological Protection Service at Sutton, Surrey. There was no measurable contamination of 2 of the boys, though it was detectable in the third; it was well below the level which would endanger his health.

This was an accident that need not have happened and would not have happened if the bin of radio-active waste had been under lock and key. The authors conclude thus: "It is our considered opinion that these two officers (local and county M.O.H.s) should be informed of the location, nature, and disposal of all radio-active materials in their areas. If this involves letting them into secrets they are surely well qualified to be recipients of such confidences. They must also know whom to contact for other expert help and advice". It might be added that in the present instance they were well served. *S. Russ*

NEWCOMBE, H. B. & JAMES, A. P. **Heredity, Health, and Radiation.** *Canadian J. Pub. Health.* 1959, Apr., v. 50, No. 4, 140–46. [14 refs.]

This important review of present-day knowledge of the effects of radiation upon hereditary disease was given at the Canadian Public Health Association, May 20, 1958. Spontaneous mutations are responsible for a part of the present load of hereditary defects, amounting, according to estimates, to not less than one seriously affected individual per 100 births. How much does radiation affect this? The suggestion is that the likely effect of exposing a human population to 30r. in each generation prior to reproduction would be an eventual doubling of those defects normally maintained by recurrent natural mutations.

From natural sources we receive about 3r. to the reproductive tissues in 30 years (before the average age of reproduction); from all medical uses of radiation people in N. America probably get an additional 3r. in the same period and from fall-out about 0·1r. in 30 years if tests continue as at present.

In order to speak more certainly of all these matters the authors consider that more work is required on detailed handling procedures and planning of research programmes of test studies. One of the chief uncertainties in the estimates given arises from our ignorance of the respective roles of selection and mutation in maintaining our present load of hereditary defects. *S. Russ*

DOBSON, J. N. **Radioactivity in Ennerdale Rural District.** *Med. Officer.* 1959, May 15, v. 101, No. 20, 275–7.

This article arises out of an accident at the Windscale works [Ennerdale Lake District] of the United Kingdom Atomic Energy Authority in 1957. The reactors came into operation in 1950; in 1952 there was a spontaneous release of heat energy, due to the so-called "recovery" of graphite from the effects of prolonged neutron bombardment; in future it would have to be dissipated deliberately at intervals. The ninth of these releases was due on October 7, 1957. As it appeared not to be proceeding, a second nuclear heating was applied, which caused overheating and failure of one or more cartridges. This was shown by rising graphite temperatures, rising activity in the pile stack meter on October 10 and a radio-active rise in the vicinity to 13·5 times the maximum permissible level for lifetime exposure. This called for precautionary action in the surrounding district.

On October 12 milk distribution from nearby farms was stopped, and the milk ban was later extended to an area of some 200 square miles. The general awareness of urgency duties by those entrusted with the general care of public safety may be gauged from the following paragraph: "There followed a discussion with the County Medical Officer on the position, the first of many with officers concerned. My notes record also talks with the Scientific Advisory Officer and the Regional Controller of the Ministry of Agriculture, Fisheries and Food, the Regional Milk Officer, the head of the Health Physics Section of the AEA Industrial Group Health and Safety Branch, the Divisional Veterinary Officer, the Deputy Works General Manager and many others".

There would have been a major disaster had it not been for the skill, resolution and devotion to duty of the Authority's staff.

As the author states, "The Windscale incident must rank as unique, surely the costliest accident ever to take place without injury or loss of life". *S. Russ*

Atmospheric Pollution

DALY, C. **Air Pollution and Causes of Death.** *Brit. J. Preventive & Social Med.* 1959, Jan., v. 13, No. 1, 14–27, 4 figs. [11 refs.]

For each of the 83 County Boroughs of England and Wales 2 sets of data have been calculated, *viz.* (a) the amounts of different types of fuel consumed—domestic and industrial—in, or about, the year May 1951 to May 1952 and related specifically to the built-up area of each town (estimated in great detail from 6-inch maps), to give an index of the town's pollution by smoke, (b) the death rates of men aged 45–64 years in 1948–54 from bronchitis, pneumonia, respiratory tuberculosis, lung cancer, other respiratory diseases and all non-respiratory diseases. Calculation of correlation coefficients shows the highest degree of association with bronchitis followed by pneumonia, respiratory tuberculosis, lung cancer and all non-respiratory diseases—in that order—all of which show a substantial association with domestic pollution. Diagrams specifically provided for bronchitis and lung cancer show a clear upward trend in the former with the pollution indices but only a quite slight upward trend in cancer of the lung. Bringing indices of social class into the

picture (social class proportions, over-crowding, population density, education) suggests that not less than one-third of the variation in the bronchitis death rates could be attributed to air pollution and another one-third to social factors. Similar calculations for lung cancer, however, give no indication that air pollution is a major factor in its aetiology. On the other hand, some data on present smoking habits give only slight differences between groups of towns differing quite considerably in their mortality. The source of the variation is therefore obscure. An attempt has been made to measure the effect of air pollution from sulphur products by studying the power stations in or near each town. The results give no reason to suppose that proximity to a power station has any noticeable effect on bronchitis mortality. *A. Bradford Hill*

Sanitation

WATER AND SWIMMING BATHS

(Including the bacteriology of water supplies)

DEPT. SCIENT. & INDUST. RES. **Water Pollution Research 1958. The Report of the Water Pollution Research Board** [GARNER, F. H., Chairman] **with the Report of the Director of the Water Pollution Research Laboratory** [SOUTHGATE, B. A.]. pp. v + 113, 59 figs. & 4 pls. [Refs. in footnotes.] 1959. London: H.M. Stationery Office. [7s.]

This is the Twenty-Sixth Report of the Water Pollution Research Board. In order to improve the coordination of research on the prevention of pollution 2 new committees have been formed, 1 with the River Boards' Association and the Scottish River Purification Boards' Association and the other with the Institute of Sewage Purification. These are in addition to the committee mentioned in the last annual Report which includes members nominated by the Federation of British Industries. In order to publicize the advances in knowledge, particularly perhaps to the smaller industrial firms, the Laboratory now undertakes the preparation of a quarterly series of short leaflets, *Notes on Water Pollution*, which are being widely distributed as a free issue.

The Report of the Director of Water Pollution Research contains clear descriptions of the mass of scientific and technical information which has been obtained by many investigations during 1958. The work, first reported in the 1957 Report [this *Bulletin*, 1958, v. 33, 771], on the identification and determination of the concentration of the chief classes of organic compounds in sewage of domestic origin, has been continued. The activated-sludge process has been studied further to obtain information on its action at high rates of aeration and low periods of retention and also to study the efficiency of aeration by bubbles of diffused air.

Synthetic detergents have received much attention in regard to their effects on sewage in reducing the absorption coefficient for oxygen in a diffused air plant; the deviations from the normal which they bring about in the biological population of sewage during activated-sludge treatment and their foaming properties. Of particular interest are the results of preliminary experiments with a new synthetic detergent, an anionic surface-active material—a new type of alkyl benzene sulphonate—which are very encouraging and suggest that it would not have the disadvantage of the detergents at present in general use.

In the section on Industrial Waste Waters there is described the continuing experiments on the biological treatment of solutions of sodium cyanide and of the complex cyanides of zinc, cadmium and copper; on coke oven effluents including the breakdown of phenolic constituents by a strain of *Pseudomonas pyocyanea*; on settled slaughterhouse waste and also on spent wash from the distillation of whisky by anaerobic digestion. Some tests were also carried out by request on the effect of ship-cleaning detergents on the condition of water in a polluted estuary. Mention is made also of short investigations carried out and advice given at factories on waste waters from egg packing and processing, the manufacture of biscuits and of chemicals, tanning and electro-deposition of metals.

Studies of the Effects of Pollution on Fish included experiments on the toxicity of zinc salts in hard and soft waters, at different temperatures and at different concentrations of dissolved oxygen. Other researches in this section concerned the toxicity to fish of chlorine and of sewage effluents containing detergents; the tolerance of roach and perch for sea-water; the effect of suspended solids on fish; and the reactions of fish in a temperature gradient.

In the investigations on Fresh-Water Streams much interesting work was done on many points of importance. Among these were a temperature survey of a heated river, an oxygen survey of a polluted stream and studies of the effect of water weeds on oxygen balance in streams. The long-term study of the fate of radio-active substances in natural waters, mentioned in the last Report, has been continued. "The work has included measurements of the effect of fall-out activity in rain on the activity of water and plants in a local river, and laboratory-scale tracer experiments on the uptake of radioisotopes by aquatic plants and bottom deposits."

During the year most of the work on the Thames Survey has been directed towards writing the final Report, but also more detailed examination on the distribution of oxidized nitrogen in the estuary was made.

In the section on Automatic Equipment there is an account of some technical aspects and of experience with

the automatic recorder for dissolved oxygen described in previous Reports, an automatic recorder for determining the proportion of oxygen in a mixture of gases and an automatic counter for measuring low levels of β activity in water.

Appendices to this Report set out (1) the publications during 1958 arising out of the work of the Water Pollution Research Laboratory, (2) the membership of the committees and (3) the senior staff of the Water Pollution Research Laboratory during 1958.

M. E. Delafield

BOUILLAUD, R. Numérations microbiennes en milieu liquide. Application à la colimétrie des eaux par une méthode statistique d'estimation. [**Enumeration of Bacteria in Liquid Media. Application to the Estimation of Coliform Organisms in Water by a Statistical Method**] *Rev. d'Hyg. et de Méd. Sociale.* Paris. 1958, Oct.–Nov., v. 6, No. 7, 731–47, 3 graphs.

The author describes the mathematical principles underlying the estimation of numbers of coliform organisms by the "most probable number" method. He then proposes a routine method for measuring pollution of water by dividing 100 cc. of water into 8 portions of varying amounts, culturing and subculturing the positive tubes or flasks to identify the type of organism. Waters containing faecal *Escherichia coli* are rejected, and the pollution of other water is measured by calculating the most probable number of *Clostridium welchii* and enterococci.

P. Armitage

CHAMBON, M. Essai sur la détermination de la pollution et de l'auto-épuration d'un fleuve. Le Rhône au cours de sa traversée de l'agglomération lyonnaise. [**A Study of the Pollution and Self-Purification of the River Rhône**] *Rev. d'Hyg. et de Méd. Sociale.* Paris. 1959, Jan.–Feb., v. 7, No. 1, 7–29, 8 figs.

This paper is an extract from a report presented in 1958 to the Departmental Commission on Water Pollution in Lyons. There is a full description with many tabulated details of the results of bacteriological and chemical analyses of samples of water taken from the rivers Rhône and Saône at different points.

In the conclusions it is mentioned that although no previous study comparable to the one here described has been carried out it is possible that the use of domestic and industrial detergents nowadays inhibits the natural self-purification of rivers. The main analytical results of this survey have been to show the extreme degree of pollution of these rivers at certain points.

These analyses and their repetition in the future will provide a scientific basis for projects to set up future works for water purification and for sewage treatment.

M. E. Delafield

UNGER, H. Radioaktivität und Wasser. Erfahrungsbericht der Staatl. Überwachungsstelle auf Radioaktivität an der Staatl. Bakteriologischen Untersuchungsanstalt München. [**Radioactivity and Water. Progress Report of the State Radioactivity Control Organization in the State Bacteriological Institute in Munich**] *Öffentl. Gesundheitsdienst.* Stuttgart. 1959, v. 21, No. 1, 16–25, 2 maps & 1 chart.

There was a time when the German spas prided themselves on the strength of the radio-activity of their waters; modern opinion is that the less the better.

The author is concerned with water for drinking purposes and has carried out an extensive series of quantitative tests on such waters in the Munich district. The paper is not of general outside interest in this respect but the author draws attention to the large variations in radon content of these waters when tests are continued over a long period, in the present instance a period of about 1 year, and this finding puts a lot of doubt in the value of the isolated measurement. It would appear, however, that a trustworthy and practical period of measurement should extend over at least a fortnight.

The author was unable to detect any direct correlation between the radio-activity of deep underground water and the external precipitation, by way of rainfall or snow.

S. Russ

SEWAGE, TRADE WASTE AND REFUSE DISPOSAL

ORFORD, H. E. & MATUSKY, F. E. **Comparisons of Short-Term with 5-Day BOD Determinations of Raw Sewage.** *Sewage & Indust. Wastes.* Wash. 1959, Mar., v. 31, No. 3, 259–67, 1 fig. [10 refs.]

The investigators of the Royal Commission on Sewage Disposal (1898) deduced that the measurement of BOD for a 5-day period minimized errors which occurred when the BOD was measured for shorter periods.

The present authors find, however, that for raw and settled domestic sewage the 20°C. BOD test can be shortened to 2 days without any serious loss in the reproducibility of the results. The paper describes a statistical analysis of the results of BOD tests on 14 different sewage samples, the BOD being measured at 20°C. for 1, 2, 3 and 5 days and at 37°C. for 1 and 2 days for each sample. For plant control the authors suggest the use of the 1 day 20°C. BOD.

There appears to be no advantage in using a temperature of 37°C. for shorter-term BOD tests as the variations in the 37°C. test for 1 and 2 days are greater than those for the corresponding 20°C. test.

The authors supply conversion factors, deduced from this work, which can be used for computing 5-day BOD values from the results of short-term tests. They state that these conversion factors should, however, only be used for wastes with a rate of oxidation similar to that of domestic sewage.

The paper contains an excellent review of the literature published, on the comparison of short-term and standard 5-day BOD tests. *D. Jenkins*

STUEWER, U. Synthetische Waschmittel und ihre Auswirkung auf Kläranlagen und Vorfluter. [**The Effects of Synthetic Detergents on Sewage Purification**] *Städtehyg.* Uelzen/Hann. 1959, May, v. 10, No. 5, 85–91, 8 figs. [16 refs.]

This is a general account of the problems resulting from the ever-increasing use of synthetic detergents. The nuisance of foaming as it exists in various places in Germany is described with some photographs. Sections of the paper deal with the chemical nature and behaviour of these detergents; the extent to which their use has increased in Germany, England and America; and their adverse effect on biological purification of sewage. There is some description of the prevention of foaming by water spraying and the use of anti-foam materials.

The problems associated with synthetic detergents are considerable and are likely to become more urgent but manufacturers of these detergents have hitherto not been cooperative although a new and less harmful detergent which has been mentioned in the English literature [see Dept. Scientific & Indust. Research Report, p. 915] has given promising experimental results. Free use has been made in this paper of references to work published in England where it is stated by the author much more scientific research on synthetic detergents has been carried out than in Germany. [See also this *Bulletin*, 1957, v. 32, 1080.] *M. E. Delafield*

MÜLLER, Gertrud. Tuberkelbakterien im Schlamm mechanisch-biologisch arbeitender Abwasserreinigungsanlagen. [**Tubercle Bacilli in Sewage Sludge**] *Städtehyg.* Uelzen/Hann. 1959, May, v. 10, No. 5, 96–7, 1 fig. [13 refs.]

The extensive use of sewage and sewage sludge as a fertilizer makes the question of the survival of pathogenic organisms in these materials an important one. Reports on the presence and survival of tubercle bacilli in the sewage from institutions for the tuberculous have been published and 1 of these reported that the bacilli could be recovered from a field where radishes were grown 4 to 5 months after the infected sewage had been applied.

In the present paper investigations on sewage and sludge from a municipal sewage works are described. Large samples—500 cc. in the case of crude sewage and 10 gm. of various sludges—were examined by cultural methods which are stated.

The results of these experiments are described and set out in a table. Among these results were:—tubercle bacilli were present in 90% of samples of crude sewage, 82% of fresh sewage sludge, 50% of activated sludge, 44% in 30-day-old sludge from drying beds and 50% of unheated mechanically precipitated digested sludge. In no instance, however, were tubercle bacilli isolated from the mechanically digested sludge when this had been kept at a temperature of about 30°C. during digestion. *M. E. Delafield*

REEVES, J. B. **Sanitary Aspects of Composted Sewage Sludge and Sawdust.** *Sewage & Indust. Wastes.* Wash. 1959, May, v. 31, No. 5, 557–64, 5 figs. [15 refs.]

A compost prepared by mixing digested sewage sludge with hardwood sawdust yields a product resembling leaf mould in appearance, texture and odour. It is beneficial to the land and offers a simple method of disposal of an otherwise objectionable and troublesome waste so long as it does not involve health hazards. Bacteriological examination of such a compost, where the samples were taken at various depths, showed however that it was not free from potential pathogens. In the study reported in this paper 61 strains of salmonellae and 12 strains of shigellae were isolated from air-dried sludge and hardwood sawdust. During one stage of the investigation a sewage effluent was used to moisten the compost and at once there was a dramatic increase in the number of salmonella and shigella isolations. The identification of the organisms was presumptive only, in accordance with their biochemical reactions, and serological tests were not employed. More detailed study is obviously indicated, but this preliminary report clearly suggests that the uncontrolled use of such a compost could constitute a danger to health. *H. J. Bensted*

HEUKELEKIAN, H. & BALMAT, J. L. **Chemical Composition of the Particulate Fractions of Domestic Sewage.** *Sewage & Indust. Wastes.* Wash. 1959, Apr., v. 31, No. 4, 413–23.

Infestation and Disinfestation

MINISTRY OF AGRICULTURE, FISHERIES AND FOOD. **Infestation Control. A Service to Agriculture and Food Storage.** pp. iv + 32, 1 fig. & 12 pls. 1958. London: H.M. Stationery Office. [4s.]

This attractively produced booklet sets out the history of rodent and insect infestation control in Great Britain, from the Ground Game Act of 1880 to the setting up of a special unit during the Second World War, and its

subsequent development. The work is now carried out by the Infestation Control Division of the Ministry of Agriculture, Fisheries and Food, and a regional service has been operating since 1957.

The greater part of the booklet describes the problems facing the Division: of insect pests in stored products, the control of rats and mice, and the control of rodents and birds harmful to crops. The variety of work described is impressive. Insect infestations are mainly in stores of flour, grain, dried fruits and nuts, and in flour mills, farms and food factories. The development of control measures against rats and mice in warehouses and sewers is outlined and there is also a short account of myxomatosis in Great Britain.

There is a reference list of scientific papers published by members of the unit since 1943.

B. R. Laurence

Food and Nutrition

FOODSTUFFS

Composition and Bacteriological Control

MEYER-OSCHATZ, W. Bakteriologische Untersuchungen zur keimvermindernden Wirkung der maschinellen Kannen- und Flaschenreinigung in der Milchwirtschaft. **[Bacteriological Investigations of Milk Can and Bottle Washing Machines]** *Ztschr. f. d. g. Hyg. u. ihre Grenzgebiete.* Berlin. 1959, Mar.–Apr., v. 5, No. 2, 65–73. [15 refs.]

The introduction to this paper is a description of the public health dangers of improperly cleaned milk containers and a short account of the methods in use in mechanical cleansing. There follows a short description of the bacteriological method employed by the author in examining the efficiency of milk vessel washing machines by determining the total viable bacterial count and the *Escherichia coli* titre of the rinse waters before and after cleansing. The names and makers of some of these machines are given but without detail of their construction. The bacteriological test results are set out in tables. Early types of machine although still used in most dairies give unsatisfactory results. Modern automatic machines are much more efficient and bring about a great reduction in the total bacterial count and an almost complete destruction of coliform organisms. At times of particular risk of milk-borne infections, disinfection by a suitable chemical disinfectant should be carried out after cleansing. Attempts should be made to devise machines which would automatically carry out both cleansing and disinfection. *M. E. Delafield*

FOOD POISONING

MASI, A. T., TIMOTHEE, R. A., ARMIJO, R., ALONSO, D. & MAINARDI, L. E. **Two Poisoning Outbreaks in Puerto Rico from Salt Preserved Codfish.** *Pub. Health Rep.* Wash. 1959, Mar., v. 74, No. 3, 265–70. [21 refs.]

Both outbreaks were thought to be due to staphylococcal enterotoxin food poisoning from salt codfish, not previously incriminated. The first outbreak, in a hospital, affected 303 persons; 10^6 per gm. coagulase-negative staphylococci only were isolated from the salt fish. It was thought possible, however, that the enterotoxin may have been produced by a coagulase-positive strain of staphylococcus destroyed by the final heating, and that the coagulase-negative strains may have been post-cooking contaminants.

In the second outbreak, 236 inmates of an institution for juvenile delinquents were taken ill, and the codfish salad yielded $1{\cdot}6 \times 10^7$ coagulase-positive staphylococci per gm.

It is suggested that partial preservation of codfish by salting does not completely destroy contaminating organisms which have a high salt tolerance, and also that the salt may serve to kill the spoilage bacteria which compete for growth with staphylococci. The hazards of exposing salted cod to water at environmental temperatures for extended periods of time is stressed.

Enterotoxin studies were carried out on cats, but the difficulties of the test and also the fact that monkeys and cats are regarded as less susceptible to enterotoxin than man were emphasised. The authors stress the urgent need for a simple, fast and reliable test for enterotoxin.

In the hospital outbreak no cultural examination of the kitchen personnel for staphylococcal carriers was made and there was no evidence of superficial purulent lesions or of upper respiratory infection.

In the second outbreak 10 of the 12 food handlers were shown to be carrying coagulase-positive staphylococci, including 6 phage-resistant strains.

The strain of coagulase-positive staphylococcus isolated from the fish salad in this outbreak was also phage-resistant. *Betty C. Hobbs*

McKILLOP, Elizabeth J. **Bacterial Contamination of Hospital Food with special reference to *Clostridium welchii* Food Poisoning.** *J. Hygiene.* 1959, Mar., v. 57, No. 1, 31–46.

Mild outbreaks of gastro-enteritis had occurred from time to time in the hospital under review. In the 6 outbreaks described there was an association between cold chicken and the usual clinical symptoms of *Cl. welchii* food poisoning, *i.e.* abdominal pain and diarrhoea within 8–12 hours of eating the suspected foodstuff.

89 samples of uncooked and 38 samples of cooked

foods were examined as purchased. Of the uncooked food 71·9% of samples were shown to contain haemolytic *Cl. welchii*, 17·9% non-haemolytic *Cl. welchii* and from 3 samples (2·2%) presumed heat-resistant strains were isolated; coagulase-positive staphylococci were found in 16·8%. From the cooked foods haemolytic and non-haemolytic *Cl. welchii* were isolated from one of 26 samples of cold meat and coagulase-positive staphylococci from 3 samples of cold meat.

Of the 173 samples of foods cooked in the hospital kitchens haemolytic *Cl. welchii* were isolated from 19·6%, non-haemolytic strains from 10·4% and presumed heat-resistant strains from 2 samples; coagulase-positive staphylococci were isolated from 11·5% of foods.

It was observed that with the exception of cold chicken, the bacterial flora was greatly reduced by cooking (colony counts were not done). 10 of 46 samples of cold cooked chicken were contaminated with fairly large numbers of *Cl. welchii*.

Experiments showed that the higher rate of contamination of chicken from the main kitchen as compared with those prepared in the special diet kitchen was related to the method of storage, which was in broth overnight between cooking and serving in the main kitchen, but removed from the broth and placed in shallow trays for 3–4 hours before refrigeration in the diet kitchen.

Immediate refrigeration of the fowls, well separated on shallow trays, was shown to be a satisfactory method for preventing the growth of *Cl. welchii*.

After investigating the cooking and handling of the fowls, the author suggests that the contamination of cooked fowls with kitchen dust might be an explanation for the presence of *Cl. welchii* rather than contamination of the uncooked bird. Of 58 samples of dust collected from floor and window ledges 89·6% contained haemolytic and 81·0% non-haemolytic strains of *Cl. welchii*.

This is an excellent and interesting piece of work.

[All workers in this field will recognize the difficulty of demonstrating heat resistance in food-poisoning strains of *Cl. welchii*, owing to the feeble production of spores, particularly in cooked poultry and other foodstuffs. Furthermore, the distinction between α- and β-haemolysis on blood agar is not always clear-cut.

The quantity of food examined is important in relation to the isolation of all intestinal pathogens; a higher percentage of positives might have been obtained if a larger sample of food had been examined.]

Betty C. Hobbs

Bacteriology and Immunity

Abstracts of papers relating to the bacteriology of plague, cholera, yaws, leprosy and certain other tropical bacterial diseases; of the rickettsial fevers; and of yellow fever, dengue, rabies and certain other tropical virus infections, are published in the TROPICAL DISEASES BULLETIN. *Their titles and page references are cited below in the appropriate sub-division of this section*

GENERAL

BUCHANAN, R. E. **Microbiological Literacy.** *Bact. Reviews.* 1958, Sept., v. 22, No. 3, 204–15.

This is an interesting and entertaining paper the scope of which is to sample and review some of "the nomenclatural pitfalls of microbiology" which "may prove stimulating, even useful, to the student (perhaps likewise to journal contributors and journal editors) in his continued groping for microbiological literacy".

The author says "Complete literacy in any field is not readily attained"; but "the acquiring of a reasonable degree of literacy in a particular field or subdivision of microbiology is quite practicable". The subject of literacy is reviewed with many good examples, in sections and subsections which concern the scientific vernacular and literacy, the construction and use of singulars and plurals, the specific epithet, the influence of modern language on spelling of modern Latin scientific names, the confusion of nomenclature and classification and the formulation of Latin descriptions and diagnoses.

The final section of the paper is entitled "Why Literacy Lapses in Microbiological Literature?"

M. E. Delafield

HABEEB, A. F. S. A. **A Study of Bacteriological Media: the Examination of Peptides in Bacto-Casitone.** *J. Pharmacy & Pharmacol.* London. 1959, June, v. 11, No. 6, 376–82.

"Three batches of Bacto-Casitone have been fractionated by the combined use of paper electrophoresis at pH 5·8 and paper chromatography in butanol-acetic acid-water system. Batches A, B and C showed 61, 73 and 73 subfractions respectively. Some of the subfractions have been found to be a mixture of few peptides while others consist of a single peptide by *N*-terminal amino acid analysis."

[See this *Bulletin*, 1959, v. 34, 557.]

YAKULIS, V. J. & HELLER, P. **Rapid Slide Technic for Double Diffusion Agar Precipitin Test.** *Amer. J. Clin. Path.* 1959, Apr., v. 31, No. 4, 323–5, 3 figs.

"A microtechnic for the performance of the precipitin test with the double diffusion method is described and its advantages emphasized. The test is based on the principle of Ouchterlony technic."

Precipitin lines can be read within 16–18 hours. Details should be sought in the original.

HARADA, K. **Volutin as a Substrate of the Gram Reaction.** *Stain Technology.* 1959, May, v. 34, No. 3, 119–23. [10 refs.]

BARTHOLOMEW, J. W., MITTWER, T. & FINKELSTEIN, H. **The Phenomenon of Gram-Positivity; its Definition and some Negative Evidence on the Causative Role of Sulfhydryl Groups.** *Stain Technology.* 1959, May, v. 34, No. 3, 147–54. [16 refs.]

MARQUIS, R. E. & GERHARDT, P. **Polymerized Organic Salts of Sulfonic Acids used as Dispersing Agents in Microbiology.** *Applied Microbiol.* Baltimore. 1959, Mar., v. 7, No. 2, 105–8, 1 fig.

Polymerized organic salts of sulphonic acids of the alkyl-aryl type—several of which are available commercially—are not injurious to biological materials and may be employed as dispersing agents in microbiology. 7 such compounds were incorporated into suspension media and shown to have no toxic effects upon *Serratia marcescens, Bacillus megaterium* and *Staphylococcus aureus.* The viability of organisms suspended in distilled water was significantly improved by addition of the dispersants. Incorporation of the agents into diluents for plate counts gave little improvement in counting efficiency if suspensions were adequately shaken. There was some effect in increasing the stability of suspensions of a number of bacteria and in promoting dispersed growth of *Mycobacterium phlei* in fluid medium. Pellicle formation by *B. subtilis* was not inhibited by the presence of the dispersants and the redispersion of centrifuged cells of *Escherichia coli* was not facilitated. [The paper serves a useful purpose in directing attention to these dispersing agents but the demonstration of their value to the microbiologist is not very convincing and the list of suggested uses would be more impressive if backed by experimental work. The reasoning behind the suggestion that these agents may usefully be employed to stabilize the controls in serological agglutination tests is difficult to appreciate.]

John R. Norris

DAVIES, R. **Observations on the Use of Ultrasound Waves for the Disruption of Micro-Organisms.** *Biochim. et Biophys. Acta.* 1959, June, v. 33, No. 2, 481–93, 8 figs. [32 refs.]

MARCUS, S., ANSELMO, C. & PERKINS, J. J. **Studies on Bacterial Pyrogenicity. I. Quantitative Basis.** *Proc. Soc. Exper. Biol. & Med.* 1958, Nov., v. 99, No. 2, 359–62.

The authors measured the pyrogenicity of intact organisms by injecting rabbits intravenously with autoclaved bacterial suspensions and recording the rectal temperatures developed 15 minutes, 1 hour and 2 hours after injection. A rise of 0·6°C. or more in an animal indicated the pyrogenic effect of the bacterium. A wide range of Gram-positive and Gram-negative bacteria was used. Saline suspensions were made from agar slopes incubated at 37°C. for 18 hours, and counts made in a Petroff-Hauser chamber. From these findings, suspensions of known number were made in NaCl, 5% dextrose, and Ringer's solution; portions of these suspensions were filtered through membrane filters (Millipore, type HA grid) and the filters cultured on human blood agar plates incubated at 37°C. This gave an estimate between the microscopic and viable counts. Other portions were autoclaved at 120°C. for 15 minutes and then injected into rabbits in the amount of 10 ml./kgm. At least 1,000 organisms/ml. of the most pyrogenic organism were necessary to raise the rabbit temperature. The authors found that with *Flavobacterium* (3 species) and *Achromobacter* (1 species)—the commonest contaminants in hospital distilled water—10^4 organisms/ml. had no pyrogenic effect. As in hospital, freshly distilled water collected under ordinary conditions with no special precautions to prevent airborne contamination can contain anything from 0 to 30 organisms/litre in 24 hours and as this was used for hospital preparations the authors suggest that in such cases membrane filter culture can indicate the number of bacteria present and hence act as a screen for pyrogenicity.

Elizabeth M. Harper

VANINI, G. C. & CAMPANA, C. Ulteriori ricerche sull'impiego dei filtri di glutammato di sodio per l'esame batteriologico dell'aria. [**Further Research on the Use of Sodium Glutamate Filters for the Bacteriological Sampling of Air**] *Igiene Moderna.* 1958, Nov.–Dec., v. 51, Nos. 11/12, 928–34. English summary (5 lines).

Confirming the work of Vanini [this *Bulletin,* 1958, v. 33, 157] on the sodium glutamate air filter the authors studied under hospital conditions the incidence of beta-haemolytic streptococci and *Staphylococcus aureus.* 2 lots of 250 litres of air were taken from various parts of a general hospital of 800 beds; from operating theatres, wards, treatment rooms, labour wards, outpatient departments, laboratories, corridors etc., 42 sampling points in all.

Of the 2 samples taken from each site one was cultured at once, the other retained for 1–5 days to test survival of the organisms. 1 lot was cultured on ordinary agar, and the other on a medium selective for pneumococci and streptococci, which contained rabbit's blood (in preference to horse blood because of its habitual lack of antistreptolysin). The cultures were incubated for at least 60 hours in view of the slow development on the selective medium.

The results showed (1) that there was practically no difference between the samples cultured at once and those cultured after a lapse of time; (2) in a certain number of cases pathogenic organisms, including *Staph. aureus,* and both alpha- and beta-haemolytic streptococci were isolated. The authors consider the results confirm the efficacy of the filter both quantitatively, and qualitatively. It has the advantage that samples can be taken at a considerable distance from the laboratory since the organisms remain viable during transit from the sampling point.

[Unfortunately no results are given of the findings at the various sampling points.] *W. K. Dunscombe*

LIDWELL, O. M. **Impaction Sampler for Size Grading Air-Borne Bacteria-Carrying Particles.** Reprinted from *J. Sci. Instruments.* 1959, Jan., v. 36, 3–8, 5 figs. [10 refs.]

For collecting airborne bacteria and separating them according to particle size, an instrument has been devised which consists, in effect, of 4 slit samplers arranged in series. The slit widths are respectively 0·7, 0·5, 0·25 and 0·05 cm. so that the air stream is progressively accelerated as it passes through the instrument and at each stage smaller air-borne particles are impinged. The 4 stages collect respectively particles over 18μ in diameter, those between 10 and 18, between 4 and 8 and less than 4μ. The volume of air sampled is 20 cu.ft. per. min. and 15 cm. per. min. Petri dishes are employed; in order to provide the least obstructed path for the air, the dishes for the first 3 stages are drilled in the centre, to provide annular plates, and the air stream passes through the centre. A number of tests of the instrument are reported, which suggest that between 11 and 20% of the bacterial cloud may be lost by impingement elsewhere than on the culture plates.

R. E. O. Williams

DARLOW, H. M. & BALE, W. R. **Infective Hazards of Water-Closets.** *Lancet.* 1959, June 6, 1196–200, 2 figs. [12 refs.]

There are several references in the literature to the possible dangers of infective aerosols from high flushing water closets [see for example, this *Bulletin,* 1956, v. 31, 1202]. In this particular paper Darlow and Bale describe their elegantly controlled experiments for the investigation of this problem. Using *Chromobacterium prodigiosum* as the test organism they showed that the flushing of a commonly used water-closet can produce a bacterial aerosol which is locally concentrated, but as it becomes more widespread experiences loss by dilution and by gravitation of the larger particles. Many of the particles, however, appeared to be small and tend to remain airborne; and it seems probable that they are small enough to be inhaled into the lower respiratory tract. Chlorination of the flushing water reduced the viability of the aerosol produced by the second flushing of the pan but did not prevent it. Closing the lid of the pan before flushing did not prevent aerosol formation although it had a reducing effect on the bacterial concentration by the elimination of the larger particles. The only effective method of dealing with the hazard was found to be a ventilating device which successfully eliminated aerosols.

H. J. Bensted

ALLEN, H. F. **Air Hygiene for Hospitals. I. Arrestment of Airborne and Dustborne Staphylococci by a Hospital Vacuum Cleaner.** *J. Amer. Med. Ass.* 1959, Feb. 7, v. 169, No. 6, 553–9, 1 fig. [14 refs.]

Tests were made of a canister-type vacuum cleaner (Filter Queen, model 500) to discover whether it was liable to disperse bacteria from floor dust into the air. The machine was fitted with 3 filters, the first being disposable and made of paper; it lacked, however, a disposable dust container. For the tests the effluent air was passed into a duct to which membrane-filter samplers were fitted. The test clouds were either culture sprayed from a De Vilbiss atomizer, or dried dust from the interior of used toy animals. In both tests the machine retained more than 99% of the cloud, and even with the primary filter alone over 85% was retained.

R. E. O. Williams

WEBB, S. J. **Chloramphenicol and the Survival of Airborne Bacteria.** [Correspondence.] *Nature.* 1959, Apr. 11, v. 183, 1072.

Suspensions of *Staphylococcus albus, Serratia marcescens* (*Chromobacterium prodigiosum*) and *Escherichia coli* were dispersed as an aerosol in a large rotating drum. Samples were taken at intervals and the death-rate estimated. In each case chloramphenicol-resistant variants died more slowly than their sensitive parents. The sensitive strains could be induced to survive as well as the resistant by spraying them from a 0·25% chloramphenicol solution or from a solution of *o*-aminophenol or inositol. It is suggested that these agents may be able to take the place of bound water in the protein during desiccation, and so preserve the cells from destruction.

R. E. O. Williams

BACTERIOSTATIC AND BACTERICIDAL SUBSTANCES; DISINFECTION

In this section the abstracts are arranged as far as possible in the following order:—General; Antibiotics; Other Therapeutic Substances; Disinfection.

WELSCH, M. & OSTERRIETH, P. **A Comparative Study of the Transformation of Gram-Negative Rods into "Protoplasts" under the Influence of Penicillin and Glycine.** *Antonie van Leeuwenhoek: J. Microbiol. & Serol.* 1958, v. 24, Nos. 3/4, 257–73. [Numerous refs.]

This paper is from Stanleyville, Belgian Congo, where the first-named author was on an official mission. It describes the morphological changes produced in 25 strains of 15 species of Gram-negative bacilli by suspension in solutions of penicillin in concentrations varying from 10 to 50,000 units/ml. together with 10% sucrose, and in solutions of glycine with and without sucrose. In penicillin protoplasts were obtained from all these organisms (including *Escherichia, Klebsiella, Proteus, Salmonella* and *Shigella* species) except *Chromobacterium janthinum* and *Pseudomonas pyocyanea.* To observe intermediate forms, including long filaments and swollen rods, and to avoid rapid lysis, which tended to occur despite the presence of sucrose, it was necessary to adjust the concentration of penicillin to the susceptibility of the species. Glycine, on the other hand, produced protoplasts, which tended to be smaller, from all the organisms except that transformation was slow and poor with *Proteus* species: this

difference in species susceptibility suggests different modes of action. Some observations were also made on the antigenic composition of protoplasts produced by glycine, and the relation of protoplasts to the large bodies of the L-cycle is discussed. *L. P. Garrod*

JOHNSTON, T. G. & CAZORT, A. G. **Immediate Reactions to Penicillin.** *Southern Med. J.* 1959, Feb., v. 52, No. 2, 186–9. [14 refs.]

These authors maintain that preliminary skin tests before injections of penicillin are safe, feasible and dependable. They have themselves done 7,000 such tests "Since a near fatal penicillin reaction occurred in our office in 1954". A drop of the preparation to be injected is placed on the forearm and a scratch made through it. A wheal develops within 5 minutes or less in sensitized patients. Each of 14 patients known or strongly suspected of having had previous anaphylactic reactions responded in this way, and 7 others among the 7,000 routinely tested did so. Others giving a history of alarming reactions did not, and these reactions on enquiry were considered not to have been anaphylactic. The treatment of anaphylactic reactions is briefly discussed, with emphasis on the immediate injection of adrenaline. [Unfortunately other authors maintain that fatal shock can occur in a patient reacting negatively to a skin test.] *L. P. Garrod*

CAPUTI, S., Jr. **An Anaphylactic-Type Reaction attributed to Penicillinase. Report of a Case.** *New England J. of Med.* 1959, Feb. 26, v. 260, No. 9, 432–4.

A child aged 5 was given daily procaine penicillin injections for 5 days for a sore throat after chickenpox, and developed urticaria. This was regarded as a reaction to penicillin, and she was given 800,000 units of penicillinase intramuscularly. A shock-like state developed within a few minutes, with a very low blood pressure, dyspnoea and cyanosis, and a large area of swelling and redness at the site of injection. Recovery was rapid after an injection of adrenaline. *Staphylococcus aureus* was apparently cultivated from the throat [although the actual statement made is that cultures were "negative" for this organism] and the hypothesis put forward is that penicillinase formed during the course of a staphylococcal infection sensitized the patient to the enzyme administered therapeutically. [This ingenious but improbable idea demands at least the support of proof that this staphylococcus formed penicillinase. No such proof is offered: it is actually said to have been sensitive to penicillin, although the significance of this is somewhat diminished by the statement that it was "very sensitive" to several other antibiotics.] *L. P. Garrod*

YAFFEE, H. S. **Erythema Multiforme (Stevens-Johnson Syndrome) Caused by Penicillin.** *Arch. Dermat.* 1959, May, v. 79, No. 5, 591.

"A 22-year-old white man with severe exudative erythema multiforme without visceral complications, probably caused by penicillin, recovered completely after treatment with intravenous corticotropin (ACTH)."

STACHIEWICZ, E. & QUASTEL, J. H. **Effects of Dihydrostreptomycin on Amino Acid Incorporation into the Proteins of *M. tuberculosis* (BCG).** *Canadian J. Biochem. & Physiol.* 1959, May, v. 37, No. 5, 687–97, 4 figs. [15 refs.]

WATSON, K. C. **Effect of Chloramphenicol on Qualitative Aspects of Antibody Production Against Enterobacteriaceae.** *J. Lab. & Clin. Med.* 1959, May, v. 53, No. 5, 743–50. [16 refs.]

Inadequate chloramphenicol treatment of enteric fever may be one cause of the considerable increase noted in the incidence of clinical relapses. It may well be related to the inadequate period during which the drug is exhibited rather than the actual dosage employed. The author draws attention to the fact that clinical relapse usually occurs at a stage of the illness when the antibody can be expected to be, and often is, reasonably high [this *Bulletin*, 1957, v. 32, 836].

Experiments showed no difference in antibody production between chloramphenicol-treated and control rabbits under immunization programmes. It was observed that a series of patients with enteric fever treated by other workers with chloramphenicol alone had a relapse rate of 14% whereas another series treated with chloramphenicol plus cortisone had a relapse rate of only 7%. A possible explanation offered by the author, is that chloramphenicol favours phagocytosis of the typhoid bacillus at the optimum blood-level of the drug and its too early withdrawal and fall in the blood-level results in the growing out of the phagocytosed bacilli with a recurrence of the bacteraemia. Cortisone depresses phagocytosis so that fewer bacilli gain the intracellular protection against the drug and consequently a reduced number of organisms are available for the initiation of the relapse phase. *H. J. Bensted*

HIRSCH, H. A., KUNIN, C. M. & FINLAND, M., with the technical assistance of Clare WILCOX & Ann NAJARIAN. **Antibacterial Activity of Serum of Normal Men after Oral Doses of Erythromycin Propionate and Triacetyloleandomycin.** *New England J. of Med.* 1959, Feb. 26, v. 260, No. 9, 408–12, 2 figs. [11 refs.]

A single dose of 500 mgm. of either erythromycin propionate or triacetyloleandomycin was given to 8 normal young men 2 hours before breakfast and blood was taken for antibiotic assay 2, 4, 8, 12 and 25 hours after the dose. The antibiotic content was assayed in 3 ways; by a falling dilution method with a streptococcus and a staphylococcus and by the cup-plate method with *Sarcina lutea*. The results of this simple experiment are presented in several different ways in both graphs and tables, allowance being made for the degree of sensitivity of each assay organism to each antibiotic: erythromycin was 7 times as active as oleandomycin against the streptococcus and rather more than twice as active against the staphylococcus. It seems that in terms of actual concentration attained in

the plasma triacetyloleandomycin reached a higher average peak level (3·4 μgm./ml.) than erythromycin propionate (2·1 μgm./ml.) and produced almost exactly the same "total activity" (area under the graph of blood concentrations). On the other hand, in terms of actual antibacterial activity the blood levels produced by erythromycin propionate were at all times considerably higher, because the minimum inhibitory concentrations of erythromycin for each organism are less than those for oleandomycin. *L. P. Garrod*

ELLIOTT, H. J. & HALL, W. H. **A Comparison of Erythromycin with Oleandomycin in Combination with Other Antibiotics against Hospital Staphylococci.** *J. Lab. & Clin. Med.* 1959, Mar., v. 53, No. 3, 364–75. [13 refs.]

These observations were made with 30 strains of hospital staphylococci, most of which were resistant to penicillin and tetracycline. The first series of experiments consisted of determining the minimum bacteriostatic and bactericidal concentrations for these organisms of erythromycin, oleandomycin and 3 proprietary mixtures of oleandomycin with tetracycline or penicillin. Erythromycin was the most active of these, but the mixtures were more effective than their individual constituents. The authors then proceeded to study the combined action of these and various other antibiotics by the right angle paper strip method, with replica plates to detect bactericidal action. There are no illustrations of such cultures, and it is therefore not clear how distinct were the observed differences. The findings are presented in various ways in a series of Tables. "True synergism" was never seen and antagonism was uncommon: various subsidiary conclusions were reached for which the original paper should be consulted. *L. P. Garrod*

EISENBERG, G. M., WEISS, W. & FLIPPIN, H. F. **Kanamycin. *In vitro* Activity against Selected Problem Pathogens.** *Amer. J. Clin. Path.* 1959, Mar., v. 31, No. 3, 267–72.

Nutrient agar plates containing different concentrations of kanamycin were inoculated by streaking with a 3 mm. loopful of undiluted broth culture of multiple strains of 5 varieties of "problem" bacteria, most of which had recently been isolated from clinical material.

The minimum inhibitory concentrations in μgm./ml. found to inhibit the growth of a majority of the strains were for *Klebsiella* spp. (94 strains) 5–10, *Staphylococcus aureus* (107) 20–40, *Salmonella* spp. (37 strains in text, 35 in table of results: some were stock cultures obtained from elsewhere) 40, *Proteus* spp. (91) >40, *Pseudomonas pyocyanea* (26) >40. Some tube dilution tests were also done with 2 inocula differing by 10-fold, with similar results, except that the minimum inhibitory concentrations tended to be lower, particularly with the smaller inoculum. The authors consider that kanamycin shows some promise, particularly for the treatment of *Klebsiella* infections.

[These results make kanamycin appear to be considerably less active than has been reported elsewhere. This may have been due at least in part to the use in the main tests of a very heavy inoculum, and to the fact that "The presence of even 1 colony was considered to represent growth of the test organism". How often such very scanty growth was obtained is not stated.] *L. P. Garrod*

MARTY, E. W., Jr. & MCCOY, Elizabeth. **The Chromatographic Separation and Biological Properties of the Oligomycins.** *Antibiotics & Chemotherapy.* New York. 1959, May, v. 9, No. 5, 286–93, 3 figs. [10 refs.]

"An experimental column chromatographic procedure for the separation of the oligomycins is presented. Paper and column chromatography showed that two major types of oligomycin complexes have been produced by fermentation—one complex containing oligomycins A and B, and the other containing oligomycins A, B, and C. Chemical and physical data that prove the existence of the individual oligomycins are also presented.

"The biological activities of the individual oligomycins were compared. It was found that these antibiotics are generally fungistatic and that they are active against many filamentous fungi, including many plant pathogens. Against the filamentous fungi, the general order of activity was oligomycin A > oligomycin B > oligomycin C. However, the human pathogen, *B. dermatitidis*, was equally and very highly sensitive to all of the oligomycins. The toxicity of oligomycin C for mice (LD_{50} 8·3 mg./Kg.) was three to four times less that of either oligomycins A or B."

MISIEK, M., GOUREVITCH, A., HEINEMANN, B., CRON, M. J., WHITEHEAD, D. F., SCHMITZ, H., HOOPER, I. R. & LEIN, J. **Mycorhodin, a New Antibiotic.** *Antibiotics & Chemotherapy.* New York. 1959, May, v. 9, No. 5, 280–85. [12 refs.]

"Mycorhodin, a new crystalline antibiotic with indicator properties, produced by an unidentified *Streptomyces* culture, is active principally against gram-positive bacteria and *Mycobacterium tuberculosis*. The production, isolation, and properties of mycorhordin are presented. In vivo activity against *Diplococcus pneumoniae* and *Staphylococcus aureus* was demonstrated with the antibiotic given either intramuscularly or orally.

"Pharmacological studies indicated severe toxic effects in dogs after five weeks of continuous administration at 20 mg./Kg./day."

EATON LABS. **Nitrofuran Biologic Bibliography, 1957.** 105 pp. [1959.] Norwich, New York.

MAZZACCA, G., ALTUCCI, P. & TALARICO, L. Aspetti dell'attività antibatterica dei derivati alchilici degli acidi solfonici. [**Antibacterial Activity of Alkyl Derivatives of Sulphonic Acids**] *Riv. Istituto Sieroterap. Ital.* 1959, Mar.–Apr., v. 34, No. 2, 120–30, 8 graphs. [20 refs.]

The English summary appended to the paper is as follows:—

"The influence on bacterial growth of two cytostatic drugs, namely Chloroethyl and Fluoroethyl-methansulphonate (alkyl derivatives of sulphonic acids) was tested.

"Bacteriostatic activity, more evident toward *E. coli* than toward *Staph. aureus*, and more pronounced for the chloro- than for the fluoro-derivative, was observed.

"The two antimytotic drugs are deprived of filament formation inducing activity for *E. coli*, and are unable to affect coagulase activity of *Staphylococci*."

BERTI, T. & VISENTINI, P. Ricerche di chemioterapia antivirale. I.—Chelati di bismuto con pirocatechindisolfonato sodico. [**Investigations of Antiviral Chemotherapy. I. Chelates of Bismuth with Sodium Pyrocatechindisulphonate**] *Giorn. di Microbiol.* Naples. 1958, Jan.–Feb., v. 5, No. 1, 42–56. [37 refs.] English summary.

An investigation has been made of the antiviral activity of chelates of bismuth with sodium pyrocatechindisulphonate. Fertile eggs at the 11th day of incubation were infected by the allantoic route with 500 LD50 of Newcastle disease virus and the bismuth chelates were injected similarly in a suitable dose after preliminary determinations of their toxicity. The extent of antiviral activity was determined after incubation for 37 hours from the depression of haemagglutin titre observed in the treated eggs in comparison with the controls. Some effect was noted with chelates containing bismuth in a ratio of 1 : 1 or 2 : 1, and chemotherapeutic indices of around 20 were observed. The active chelates also agglutinated chick red cells, and it is concluded that they exerted their effect by interfering with the attachment of the virus to the cells. *D. J. Bauer*

BÖNICKE, R., with the technical assistance of E. HONIGMANN, H. RÖPCKE & H. ZANDER. Über die tuberkulostatische Wirksamkeit pentaheterocyclischer Carbonsäurehydrazide. [**The Tuberculostatic Activity of Pentaheterocyclic Carbonic Acid Hydrazides**] *Ztschr. f. Hyg. u. Infektionskr.* 1958, v. 145, No. 3, 263–75. [20 refs.]

Thiophen-2-carbonic acid hydrazide (TCH) and pyromucous acid hydrazide (BSH) were found to inhibit the growth of numerous strains of *Mycobacterium tuberculosis* of bovine type in concentrations of 0·1–0·8 μgm./ml., whereas all other mycobacteria tested, including tubercle bacilli of human and avian types, and *Myco. balnei, fortuitum, phlei* and *smegmatis*, were uninhibited by 25 μgm./ml. of either substance. Inhibition by, *e.g.*, 10 μgm./ml. should therefore serve as a new and reliable criterion of identity for bacilli of bovine type. The author has also compared the action of these substances with that of isoniazid to which they are chemically related. There is complete cross-resistance between the 3: antagonists of INH also antagonize the action of TCH and BSH, and TCH- and BSH-resistant tubercle bacilli are also catalase-negative. *L. P. Garrod*

RUDAT, K. D. Über die antibakterielle Wirkung verschiedener Fussbodenbeläge und Wandanstrichmittel und ihre Bedeutung für Klinik und Krankenhaus. [**On the Antibacterial Action of Various Floor Coverings and Wall Decorating Materials and its Significance for the Clinic and Hospital**] *Ztschr. f.d.g. Hyg. u. ihre Grenzgebiete.* Berlin. 1958, Sept.–Oct.–Nov.–Dec., v. 4, Nos. 5/6, 272–81, 7 figs.

This paper is from the Institute of Hygiene of the Humbold University in Berlin, and although not said to have been read at a meeting, begins "I speak to you today . . .", while the last paragraph begins "Ladies and Gentlemen . . .". It has almost no text headings, no Tables of results and no summary: of the 7 photographic illustrations, said originally to have been in colour, 3 are of rooms in a tumour clinic in Berlin, with legends, and 4 are of cultures of floor materials, without legends.

The argument laboriously pursued is that architects and builders should be instructed to surface rooms not only in hospitals and clinics, but in schools and other buildings where transmission of infection is important, with bactericidal materials. The author reports tests he has done himself with such materials: bacteria of 11 named species and others were applied to the material and swabbed off later to see whether they had survived, or the contaminated material itself was cultivated, or strips of the material were placed in saline, which was then inoculated, and cultures were made from this at intervals. No detailed results are given; the findings are described in vague general terms in only 1 page of text. Satisfactory bacteriostatic or bactericidal action was exerted by linoleum, cork lino, latex foam materials, and some, but not all, samples of rubber [whether synthetic or natural unstated]. On the other hand, floor and wall coverings having a "PVC basis" [?polyvinyl chloride] were inactive. *L. P. Garrod*

DUNKLIN, E. W. & LESTER, W., Jr. **Residual Surface Disinfection. II. The Effect of Orthophenylphenol Treatment of the Floor on Bacterial Contamination in a Recovery Room.** *J. Infect. Dis.* 1959, Jan.–Feb., v. 104, No. 1, 41–55, 6 figs. [35 refs.]

This experiment was conducted in a recovery room of an operating theatre suite in the Billings Hospital, Chicago. The floor of this room was mopped daily with a 2·5% solution of O-Syl, a disinfectant of which the principal constituent is orthophenylphenol: it was then "polished with an electric buffer". At other times it was treated with a detergent solution instead of O-Syl. The effect of the latter in destroying bacteria in airborne particles deposited on the floor was judged by 4 kinds of culture: (1) air counts obtained by bubbling measured amounts of air through broth, (2) air counts obtained by simply exposing culture plates for 6 hours, (3) swab samples of shelves and other surfaces apart from the floor, (4) swab samples and suction samples through broth of the floor itself. Large numbers of such observations were made and are presented in tables and diagrams. The average numbers of bacteria recovered during O-Syl treatment, compared with those while only a detergent was being used, were reduced by about 90% on the floor, 60% on untreated surfaces and 44% in the air. When an adjoining room was also treated these figures became 95, 60 and 50%. *L. P. Garrod*

MERKENSCHLAGER, M. & SCHMID, D. O. Untersuchungen zum Wesen der Beweglichkeit bei Mikroorganismen an der Wirkung von Chemotherapeutica. [**Studies on the Motility of Micro Organisms in Relation to the Effect of Chemotherapeutic Agents**] *Ztschr. f. Hyg. u. Infektionskr.* 1959, v. 145, No. 5, 481–7. [23 refs.]

The motility of both *Trichomonas foetus* and *Proteus vulgaris* was arrested by certain concentrations of 2 substances of mercaptide nature, "Bilamid" (pyridine-3-carboxy-oxymethylamide) and "Cealysin" (trimethanolmelamine). This effect was prevented by the addition of adenosine triphosphate. It is thought probable that, in both species, the action of these 2 substances is to interfere with the action of adenosine triphosphatase.

L. P. Garrod

SCHNITZER, R. J., GRUNBERG, E., DELORENZO, W. F. & BAGDON, R. E. **Triclobisonium Chloride (Triburon), an Antimicrobial Agent with Local Activity in Living Host Tissues.** *Antibiotics & Chemotherapy.* New York. 1959, May, v. 9, No. 5, 267–76. [20 refs.]

"Triclobisonium chloride, a new antimicrobial agent, is a member of a series of bisquaternary diamines derived from β-ionone. It is characterized by high bacteriostatic and moderate bactericidal activity in vitro against gram-positive and gram-negative organisms. The compound exerted a marked local antibacterial effect in subcutaneous infections in mice with all strains of β-hemolytic *Streptococcus pyogenes* and *Staphylococcus aureus* tested, regardless of their resistance to antibiotics. Activity against *Escherichia coli* in vivo was more variable, and non-susceptible strains were detected. *Ps. aeruginosa* did not respond to the drug in vivo.

"A certain activity was also observed when triclobisonium chloride was tested in local subcutaneous infections in mice with *Candida albicans* and *Trichomonas vaginalis*. These organisms as well as dermatophytes were also inhibited in vitro."

INDIVIDUAL BACTERIA

In this section the abstracts are arranged as far as possible in the following order:—General; Enteric Organisms; Corynebacterium, Mycobacterium; Staphylococcus; Streptococcus; Brucella; Haemophilus; Pasteurella; Pseudomonas; Neisseria; Donovania; Spirochaetes, Leptospira; Anaerobes; Bacillus; Others.

COMBIESCO, Cornelia, CRĂCEA, E., NICOLESCO, Marcela & REZMERIȚĂ, Constanța. Étude sur la détermination du genre Salmonella à l'aide d'un bactériophage anti-somatique. [**Investigations on the Determination of the Salmonella Genus by means of an Antisomatic Bacteriophage**] *Arch. Roumaines Path. Expér. et Microbiol.* 1958, Sept.–Dec., v. 17, Nos. 3/4, 587–93. [12 refs.]

This is a report on tests carried out on 921 salmonella strains, comprising 82 serotypes, with the late Miss CALLOW's paratyphoid B phage type 1 (FELIX & CALLOW, this *Bulletin*, 1943, v. 18, 865]. This is an O-phage to which almost all salmonellae are sensitive, but extremely few of the other Enterobacteriaceae and then only to the concentrated phage. Of the 921 salmonella strains reported here only 13 cultures were not fully sensitive to the para. B O-phage type 1, whereas 96% of the 601 strains of Enterobacteriaceae, other than salmonellae, were resistant to this phage. These results are in keeping with the experience of other workers in this field.

H. J. Bensted

MIKULASZEK, E. & DZUŁYNSKA, Janina. Chromatograficzna analiza wielocukrowców z drobnoustrojów rodzaju *Salmonella*. [**Chromatographic Analysis of Polysaccharides from *Salmonella* Strains**] *Archiwum Immunol i Terapii Dośw.* Warsaw. 1959, v. 7, No. 1, 1–13, 5 figs. [18 refs.] English summary.

MIYAKE, T. & DEMEREC, M. *Salmonella-Escherichia* **Hybrids.** [Correspondence.] *Nature.* 1959, June 6, v. 183, 1586.

NICOLLE, P., HUET, M. & NINARD, B., with the technical collaboration of H. ROUSSEL, Jacqueline BRAULT, Janine MARTIN & Anne M DU PLESSIS. Les lysotypes du bacille typhique identifiés en Afrique du Nord. [*Salmonella typhi* **Phage Types Identified in North Africa**] *Arch. Inst. Pasteur de Tunis.* 1958, June, v. 35, No. 2, 153–77.

The greater part of this paper is taken up with an account of the development of epidemiological methods for the study of outbreaks of typhoid fever: the discovery of the Vi antigen, the introduction of the Vi-phage typing methods and the exploitation of these procedures to make it one of the most valuable tools available to the epidemiologist. The authors give due credit to FELIX, CRAIGIE and others for their achievements, but as full references are not quoted, the long introduction to this article loses much of its value as a review of the literature. It is, however, of interest although very familiar to most readers.

In their survey of the distribution of phage types in French North Africa the authors attempt a further classification by studying the fermentation reactions of the strains isolated on xylose and arabinose; by this means they define 4 sub-types according to the reactions obtained with these 2 sugars. The great majority of the strains fermented xylose but were not found to attack arabinose (type 1), strains not fermenting either sugar (type 2) were next in order; other combinations of results were very rare.

It is not feasible here to consider the detailed findings of this survey but it may be of interest to record that out of a total of 1,619 cultures examined more than one-third belonged to type E_1 and one-fifth were classified as Vi degraded forms (Felix). With regard to important differences in the distribution of *Salmonella typhi* phage types in the 3 countries comprising French North Africa, it was found that type A was predominant in Algeria, but comparatively uncommon in Morocco.

Type C, was much less common in Tunisia than in the other 2 countries. In Morocco, especially in the Fez region, types L_1 and L_2 were found with some frequence.

Further and wider experience of the biochemical typing scheme is required before its value as a complementary classifying method can be assessed.

The phage typing work reported here was controlled with standardized reagents prepared by the Reference Laboratory of the International Committee for Enteric Phage Typing which was founded by Felix.

H. J. Bensted

MITSUHASHI, S., HARADA, K. & KAWAKAMI, M. **Studies on the Experimental Typhoid. IIa. Relation between Virulence and Antigenic Structure of Virulent and Attenuated Strains of** *S. enteritidis*. *Japanese J. Exper. Med.* 1959, Feb., v. 29, No. 1, 1–8. [12 refs.]

From an original R-form of *Salmonella enteritidis* some apparently smooth colonial forms were obtained after serial passage through broth. The sugar reactions of the two forms were identical and it was found that the degree of S—R variation ran parallel to the mouse virulence. The antigenic formulae were found to be: S-form—$9.12_1.12_2.12_3$.gm.; R-form—9a.(9b).12_1.gm.

H. J. Bensted

KRIEG, N. R., WEDBERG, S. E. & PENNER, L. R. **The Cockroaches** *Blaberus craniifer* **and** *Blaberus discoidalis* **as Vectors of** *Salmonella typhosa*. *Amer. J. Trop. Med. & Hyg.* 1959, Mar., v. 8, No. 2, Pt. 1, 119–23, 3 figs. [10 refs.]

The authors developed an elegant technique for mounting or holding cockroaches for controlled feeding experiments and the collection of material for testing. It was found that whereas *Salmonella enteritidis* survived passage through the gut of cockroaches with regularity, survival in the case of *Salm. typhi* was but rarely demonstrated and only when the holding time was very short. Further investigation suggested that the failure of *Salm. typhi* to survive the passage was associated with the very low *p*H of the fluid in the crop of these roaches as compared with the rest of the gut; a number of estimations showed that the *p*H of the crop fluid varied from 3·9 to 4·4. The critical *p*H for survival of *Salm. typhi* was found to be 4·51 and the period of exposure 6 hours. *Salm. enteritidis* can survive in a more acid medium. Organisms which appeared to be related to the propionibacteria were isolated from the crops of these cockroaches and it was concluded that these lactobacillus-like organisms, which can flourish in their crops, are responsible for the failure of the typhoid bacillus to survive passage through the gut of cockroaches although other salmonellae are unaffected by the high acidity.

H. J. Bensted

TOMA, S., SORU, E., BARBER, C., GRITAENCO, V. & BOGOKOWASKY, B. Contribuţii la studiul vaccinurilor antitifo-paratifice din extracte microbiene adsorbite pe suport mineral. I. Studiul imunobiologic comparativ al unor extracte antigenice obţinute din *S. typhi* si alte Enterobacteriacee conţinînd antigen *Vi*. [**Contributions to the Study of Typhoid-Paratyphoid Vaccines prepared from Bacterial Extracts Adsorbed on a Mineral Support. I. Comparative Immunobiological Study of Antigenic Extracts obtained from** *Salmonella typhi* **and other Enterobacteriaceae containing Vi Antigen**] *Studii si Cercetări Inframicrobiol., Microbiol. si Parazitol.* 1958, v. 9, No. 1, 107–22. [27 refs.] French summary.

An investigation has been made of the antigenic properties of extracts of *Salmonella typhi* and related organisms containing Vi antigen made by extraction with hot water, hot O.25 *N* HCl or trichloracetic acid. The antigens contained in the extracts were studied by precipitin tests and by the active immunization of rabbits. The trichloracetic acid extract contained O and Vi precipitinogens, but was very toxic and produced only low titres of Vi antibody in rabbits. Hydrochloric acid extracts contained Vi precipitinogen, were not toxic, and regularly caused the production of Vi antibody in titres of 160–320 in rabbits. Aqueous extracts contained the full complement of antigens of the strains from which they were prepared, were moderately toxic and gave rise to O, H and Vi antibodies in high titres.

D. J. Bauer

NICOLESCO, Marcela. Étude sur les caractères biologiques des souches qui entrent dans la composition du vaccin T.A.B. [**A Study concerning the Biological Characters of the Strains included in T.A.B. Vaccine**] *Arch. Roumaines Path. Expér. et Microbiol.* 1958, Sept.–Dec., v. 17, Nos. 3/4, 401–16. [43 refs.]

The English summary appended to the paper is as follows:—

"1. The study of 'S'—'R', agglutinating, and biochemical characters of typhoid and paratyphoid strains is of a certain importance, although these characters are not determinant for the preparation of T.A.B. vaccine.

"2. Among the strains of S. typhi, S. paratyphi A, and S. paratyphi B subjected to investigation, paratyphoid B bacilli were found to display the highest degree of virulence; they were followed by typhoid bacilli, while paratyphoid A bacilli were the least virulent.

"3. As regards toxicity in mice, the strains of S. paratyphi A and B display a higher degree of toxicity than the strains of S. typhi.

"4a. The immunogenicity test disclosed that 75% of the S. typhi and paratyphi B strains are immunogenic, while among 11 investigated strains of S. paratyphi A, one only gave positive results.

"b. The passive protection test disclosed that sera prepared by means of living typhoid bacilli were more efficient than those prepared by means of heatkilled bacilli, while sera prepared by means of suspensions of paratyphoid B bacilli displayed a stronger protecting action than those prepared by means of S. paratyphi A strains.

"5. By comparing the virulence, toxicity, immunogenicity, and agglutinability of a series of S. typhi, S.

paratyphi A, and S. paratyphi B strains, it was established that:

"*a*) All highly virulent strains of S. typhi were immunogenic.

"*b*) All the S. typhi strains displaying a low Vi agglutinability had a low virulence and were but feebly immunogenic.

"*c*) No relationship could be found to exist between virulence and toxicity, between toxicity and immunogenicity, between virulence, toxicity, and immunogenicity on the one hand and O agglutinability on the other hand, between all these characters and the phage type.

"*d*) No relationship could be found to exist between the virulence, toxicity, and immunogenicity of S. paratyphi A strains and their agglutinability by anti-O sera.

"*e*) There was a close correlation between virulence, toxicity and immunogenicity in S. paratyphi B strains, but no relationship could be found to exist between these characters and the agglutinability of the strains.

"6. No definite relationship could be found to exist between the virulence, toxicity and immunogenicity on the one hand, and the agglutinability by Vi sera in S. typhi or by anti O sera in S. paratyphi A and B strains on the other hand."

GRANT, L. S. **A New *Salmonella* Type Salmonella Jamaica. – 9,12: r – 1,5.** *West Indian Med. J.* 1958, Dec., v. 7, No. 4, 249–50.

"A new *Salmonella* type, *Salmonella jamaica* = 9, 12: r – 1, 5. isolated from human faeces and causing gastro-enteritis is reported."

ISTRATI, G., MANOLIUM, N. & GOREA, A. Bakteriendissoziation. V. Die Antigenstruktur von Shigella-Ro-Formen. 1. Teil. Untersuchungen an sechs Stämmen mit der Serumagglutination sowie der direkten und gekreuzten Absorption der Agglutinine. [**Bacterial Dissociation. V. The Antigenic Structure of Ro Forms of *Shigella*. 1st. Part. Investigation of Six Strains by means of Serum Agglutination and of Direct and Crossed Agglutinin Absorption**] *Arch. Roumaines Path. Expér. et Microbiol.* 1958, Sept.–Dec., v. 17, Nos.3/4, 435–48, 12 figs. [20 refs.]

The English summary appended to the paper is as follows:—

"The antigenic structure of six strains of various *Shigella* species in the Ro phase was investigated. *Shigella* strains in the Ro phase display varied antigenic structures. As a rule their antigenic pattern includes a type-specific antigen and several common group-antigens. There is no direct relationship between the structure of the O antigen of undegraded and the structure of the o antigen of the same degraded strains. *Sh. flexneri* strains possessing the same O antigen may differ by their o antigen, and vice versa, strains possessing the different O antigens may possess very similar o antigens. Close relationships may be found to exist not only between strains of the same species, but between different strains of *Shigella* as well. Conversely, considerable differences are sometimes found to be present as regards the strains of the same species of *Shigella*.

"The structure of o antigens was found to be a very complex one, these antigens consisting of a considerable number of factors, some of which behave as complete antigens while others display the properties of incomplete antigens (haptens or haptids). On the basis of the data obtained, a provisional antigenic diagram of the degraded *Shigella* strains under investigation could be established, including four specific antigens and several group-antigens."

GOREA, A., WEINBACH, R., MANOLIU, N. & ISTRATI, G. Bakteriendissoziation. V. Die Antigenstruktur von Shigella-Ro-Formen. 2. Teil. Untersuchungen an sechs Stämmen mittels der indirekten Hämagglutination und deren Hemmungsreaktion. [**Bacterial Dissociation. V. The Antigenic Structure of Ro Forms of *Shigella*. 2nd Part. Investigation of Six Strains by the Indirect Haemagglutination Method and the Inhibition Test**] *Arch. Roumaines Path. Expér. et Microbiol.* 1958, Sept.–Dec., v. 17, Nos. 3/4, 563–74, 12 figs. [20 refs.]

The English summary appended to the paper is as follows:—

"The alkaline extracts of six *Shigella* strains in the Ro phase were studied by the method of indirect haemagglutination and its inhibition. The antimicrobial sera described in the first part were used for this purpose. The antigenic complexity of Ro strains as well as the absence of any direct relationship between the antigenic o structure of non-degraded and the o structure of the same degraded strains were confirmed. Alkaline extracts were shown to be formed of complete specific or group antigens and of incomplete antigens of the hapten or haptid type. One of the six extracts failed to inhibit indirect haemagglutination, although it reacted with the corresponding antisera when adsorbed onto red blood-cells. It would appear from preliminary chemical investigations that the extracts are nucleoproteins."

ŚLOPEK, S. & DĄBROWSKI, L. Nowy typ pałeczek jelitowych (4854–75) wykazujący pokrewieństwo antygenowe z pałeczkami *Shigella flexneri*. [**A New Type of Enterobacteriaceae (4854–75) showing Antigenic Relationship with *S. flexneri***] *Archiwum Immunol. i Terapii Dośw.* Warsaw. 1958, v, 6, No. 1, 93–102. English summary.

A new type of organism (strain 4854–75) belonging to the Enterobacteriaceae has been isolated from the stools of a boy living in contact with typhoid infection. It fermented glucose, sometimes with gas formation, and mannitol, xylose, arabinose, rhamnose and glycerol, but not lactose, dulcitol, sorbitol, maltose or sucrose. It did not form indole or hydrogen sulphide and did not decompose urea. The Voges-Proskauer test was negative and the methyl red and Wood and Baird tests were positive. The strain contained heat-labile group and heat-stable type antigens and showed an antigenic

relationship with *Shigella flexneri*. The heat-labile antigen (δ antigen) had not been previously encountered in the Enterobacteriaceae. *D. J. Bauer*

ŚLOPEK, S. & DABROWSKI, L. Nowy typ pałeczek jelitowych (4486–65) wykazujacy pokrewieństwo antygenowe z pałeczkami *Shigella* i *alkalescens-dispar*. [**A New Type of Enterobacteriaceae (4486–65) showing Antigenic Relationship to *Shigella* and *alkalescens-dispar***] *Archiwum Immunol. i. Terapii Dośw.* Warsaw. 1958, v. 6, No. 1, 103–18. English summary.

During the course of a mass survey of the occurrence of Shigella among the Polish population 12 similar strains of enteric organisms, designated group 4486–65, were isolated from the stools of [presumably healthy] adults. The strains fermented glucose, mannitol, xylose, rhamnose, maltose, sucrose, arabinose and glycerol with the production of acid but not of gas. Lactose, dulcitol and sorbitol were not fermented. The methyl red test was positive and the Voges-Proskauer test negative, indole and hydrogen sulphide were not formed and urea was not decomposed. The strains behaved identically in cross-absorption tests, and were agglutinated by *Sh. flexneri* and *alkalescens-dispar* antisera. A hitherto unknown thermolabile antigen (γ) was detected in the strains; their antigenic relationship with *Sh. flexneri* and the *alkalescens-dispar* group was due to the presence of common thermostable antigens. The strains also possessed a type antigen with thermostable and thermolabile components. *D. J. Bauer*

ŚLOPEK, S. & DĄBROWSKI, L. Charakterystyka nowych ciepłochwiejnych antygenów wystepujacych u pałeczek jelitowych. [**The Characteristics of New Thermolabile Antigens occurring in Enterobacteriaceae**] *Archiwum Immunol. i Terapii Dośw.* Warsaw. 1958, v. 6, No. 1, 119–26. [13 refs.] English summary.

A study has been made of the thermolabile γ and δ antigens of the 4486–65 and 4854–75 strains of enteric organisms described in the preceding papers. In absorption tests with specific antisera it was found that the γ antigen was destroyed by heating at 100°C. for 2 hours and by treatment with N HCl for 20 hours at 37°C. but not by 50% ethanol under the same conditions; δ antigen was destroyed by heating and ethanol but not by HCl. The antigens also differed serologically and gave no cross-agglutination. The properties of the γ and δ antigens are compared with those of the hitherto known antigens of the enteric group in a table, from which it can be seen that they differ from all the other antigens but bear some resemblance to antigens α and β. *D. J. Bauer*

METZGER, M. Badania nad budową antygenową pałeczek *Shigella boydii*. I. Charakterystyka nowego ciepłochwiejnego antygenu. [**Studies on the Antigenic Structure of *Shigella boydii* Strains. I. Characteristics of a New Thermolabile Antigen**] *Archiwum Immunol. i Terapii Dośw.* Warsaw. 1958, v. 6, No. 1, 135–48. [41 refs.] English summary (7 lines). II. Serologiczne pokrewieństwo wśród typów *S. boydii* z uwzglednieniem ciepłochwiejnych i ciepłostalych antygenów. [**II. Serological Relationship among *Sh. boydii* Types with regard to Thermolabile and Thermostable Antigens**] *Ibid.*, 149–65. [22 refs.] English summary.

Representative strains of the 11 types of *Shigella boydii* have been examined for the presence of thermolabile antigens by agglutination tests with organisms heated at 100°C. or 120°C. or treated with 50% ethanol or N HCl and their respective antisera before and after absorption. The investigations revealed the presence of an antigen, designated antigen C, which was destroyed by heating for 2 hours at 120°C.; it resisted heating after $2\frac{1}{2}$ hours at 100°C. and was only partially affected by treatment with ethanol or N HCl. The antigen was found in all types of *Sh. boydii*, and did not inhibit the agglutination of live organisms by O antisera. The C antigen showed some serological relationship with the O antigen, in that common antigenic components could be present in a given type in either antigen or in both at the same time. The antigenic structure of the 11 types and 6 provisional serotypes of *Sh. boydii* in relation to the C and O antigens is shown in a table. *D. J. Bauer*

ISTRATI, G. & MEITERT, T. L'utilisation des sérums absorbés ("négatifs") dans le diagnostic de laboratoire des Shigelloses. [**The Use of Absorbed "Negative" Sera in the Laboratory Diagnosis of Shigellosis. The Possibility of preparing Agglutinating Antidysenteric Sera in Big Animals (Horse)**] *Arch. Roumaines Path. Expér. et Microbiol.* 1958, Sept.–Dec., v. 17, Nos. 3/4, 499–512. [26 refs.]

The expression "absorbed 'negative' sera", used by the authors, refers to artificially prepared immune sera from which the homologous agglutinins have been absorbed. It is well recognized that normal animal sera may contain natural agglutinins for many members of the Enterobacteriaceae family—a number of which it is not feasible to identify. Consequently an antidysentery serum prepared against a particular strain of *Shigella flexneri* may contain a wide variety of nonspecific agglutinins which can interfere with type identification. The authors' thesis suggests that slide agglutination tests employing raw and absorbed "negative" sera in parallel will greatly facilitate the work of identifying members of the dysentery group and further that the horse can be used to provide these sera, with all the advantages (economical) of employing a large animal for the preparation of immune sera.

[While the possibilities of this procedure are fully appreciated, it is not considered that it will greatly facilitate exact type determination of the members of the Flexner group, which is so essential for the epidemiological study of infections caused by this most important group of dysentery bacilli, neither will it help significantly where the cross reactions are due to shared antigens.] *H. J. Bensted*

METZGER, M. & OBST, Bronisława. Naturalne aglutyniny czerwonkowe w normalnych surowicach króliczych. [**Natural Dysenteric Agglutinins in Normal Rabbit Sera**] *Archiwum Immunol. i Terapii Dośw.* Warsaw. 1959, v. 7, No. 1, 53–63. [15 refs.]

The English summary appended to the paper is as follows:—

"The present studies aimed to establish some properties and the degree of the specificity of agglutinins, occurring in normal rabbit sera, for *S. flexneri* and *S. boydii bacilli*. The incidence of agglutinins for the particular types and subtypes is given in table 1. The absorption tests showed that the natural agglutinins are characterized by a high specificity; the absorption of the serum with bacilli of one kind resulted, as a rule, in the suppression of agglutinins only for bacilli used for the absorption, affecting but slightly the agglutination of other types (table 2).

"Further experiments (tables 3 and 4) revealed that the natural agglutinins are directed against the thermoresistant antigen components of *S. flexneri* and *S. boydii* bacilli, whereas no agglutinins could be found for antigens scattered more superficially in the bacterial cell and sensitive to high temperature; their presence was detected in some *S. flexneri* types by Ślopek and Dąbrowski (14), and in *S. boydii* types—by Metzger (10).

"The significance of the natural agglutinins as a factor enhancing the difficulties on studying the antigenic structure of dysentery bacilli has been discussed."

GOREA, A.; ISTRATI, G.; MĂLDĂRESCO, I. La Vaccination Antidysentérique. I. Relations entre la voie de vaccination et la voie d'infection, respectivement d'intoxication avec des germes vivants, germes mort ou extraits glucido-lipidiques de *Sh. flexneri* 2a [**Antidysenteric Vaccination. I. Relations between the Route of Vaccination and the Route of Infection or Intoxication with Living Germs, Killed Germs, or Glucidolipidic Extracts of** *Sh. flexneri* 2a] [GOREA, ISTRATI & MĂLDĂRESCO]. *Arch. Roumaines Path. Expér. et Microbiol.* 1958, Sept.–Dec., v. 17, Nos. 3/4, 359–68. II. Expériences d'immunisation des souris vis-à-vis de l'infection homologue et hétérologue avec des souches *Sh. flexneri* de types différents [**II. Immunization Experiments in Mice against Homologous and Heterologous Infection with Strains of** *Sh. flexneri* **belonging to Various Types. Non-Specific Immunization against Infection with** *Sh. sonnei* **Phase I**] [ISTRATI, GOREA & MĂLDĂRESCO]. *Ibid.*, 369–82. [27 refs.] III. Expériences avec des vaccins corpusculaires de *Sh. flexneri* 2a thermoinactivés, alcoolés, formolés et traités par l'acétone [**Experiments with Heat-Inactivated and with Alcohol-, Acetone-, or Formol-Treated Corpuscular Vaccines of** *Sh. flexneri* **2a**] [ISTRATI, GOREA & MĂLDĂRESCO]. *Ibid.*, 575–85. [28 refs.]

I. The optimal route for challenge after the immunization of mice with a dysentery vaccine depends on the route chosen for immunization. If the vaccine is injected intraperitoneally then the most striking results are obtained by intraperitoneal challenge. Intravenous immunization yields satisfactory results against an intraperitoneal challenge, but the subcutaneous route will only yield results of the same order against an intraperitoneal challenge so long as the size and number of injections are significantly increased. Mice show little or no immunity, whatever the method of immunization, against the intravenous challenge. Strains of low virulence or trichloracetic extracts of organisms proved to be poor antigens.

II. The virulence of the strain of *Shigella flexneri* used to immunize the mice is of paramount importance. As far as can be ascertained the immunity conferred depends on the virulence of the immunizing strain and not on its serotype and the protection afforded is largely non-specific within the Flexner group. On the other hand it was found that the cross immunity to smooth strains of *Sh. sonnei* occurred only when particular strains of *Sh. flexneri* were used to immunize the mice. [It is stated that the *Sh. sonnei* used for this challenge were phase I. Pure phase I *Sh. sonnei* can be highly virulent for mice whereas phase II are almost avirulent; a challenge dose of 10^9 organisms with 500 million as the control dose strongly suggests that the *Sh. sonnei*, in spite of their smooth colonial appearance, were largely composed of cells with phase II antigens so that the results have a doubtful significance.]

III. When the heat-inactivated vaccine was compared with the alcohol-, formalin- and acetone-treated preparations it was found to be more toxic to mice than the other 3. With the usual 2 immunizing injections the heat-treated, with the alcohol- and acetone-treated, vaccines gave about 50% protection in mice; the formalin-treated vaccine was less efficient. Massive doses of all the 4 vaccines injected intraperitoneally gave a considerable degree of protection against challenge by the same route, but only the heat-killed vaccine given as a single massive dose subcutaneously conferred any reasonable degree of immunity against an intraperitoneal challenge. *H. J. Bensted*

MILBAUER, Ruth & GROSSOWICZ, N. **Reactivation of Chlorine-Inactivated** *Escherichia coli*. *Applied Microbiol.* Baltimore. 1959, Mar., v. 7, No. 2, 67–70.

It was found that under certain conditions chlorine-treated bacteria could be reactivated. Washed suspensions of *Escherichia coli* were exposed in low concentration to varying doses of chlorine for different periods of time and samples withdrawn for immediate plating on nutrient agar. Treatment with 1 p.p.m. chlorine for short periods resulted in very few recoveries but suspensions exposed to the action of 0·2 p.p.m. chlorine for periods of 1 to 3 hours were found to show high reactivation rates. *H. J. Bensted*

MILBAUER, Ruth & GROSSOWICZ, N. **Effect of Growth Conditions on Chlorine Sensitivity of** *Escherichia coli*. *Applied Microbiol.* Baltimore. 1959, Mar., v. 7, No. 2, 71–4.

The authors compare the reactivation rates of *Escherichia coli* after exposure to different concentrations of chlorine for different periods [see above] when the cultures, from which the test suspensions were prepared, were grown on ordinary nutrient agar or on "minimal" agar. The formulae for the 2 media were as follows:—

Nutrient Agar		*Minimal Agar*	
Peptone (Difco)	10·0 gm.	K_2HPO_4	7·0 gm.
NaCl	5·0 gm.	KH_2PO_4	3·0 gm.
$Na_2HPO_4 : 12H_2O$	2·5 gm.	$Na_3Cit.3H_2O$	0·5 gm.
Bovril	3·0 gm.	$MgSO_4 : 7H_2O$	0·1 gm.
Bacto-Agar (Difco)	20·0 gm.	$(NH_4)_2SO_4$	1·0 gm.
Distilled Water	1000·0 ml.	Bacto-Agar (Difco)	20·0 gm.
		Distilled Water	1000·0 ml.

E. coli grown on nutrient agar were found to be much less affected by the action of the chlorine than those grown on minimal agar when the conditions of exposure were the same and this difference was more marked with the larger doses of chlorine. Chlorine is known to act as a poison to the sulph-hydryl groups and although untreated bacteria, whether grown on nutrient or minimal agar, were found to contain the same amount of SH-group, after chlorine treatment the reduction of the SH content was significantly greater with the cells grown on minimal agar than with those grown on nutrient agar. As the chlorine concentrations were increased the greater were the differences in intact SH-groups between the 2 types of bacterial cells. The SH-groups of the cultures grown on a relatively rich medium were less sensitive to the action of chlorine than those grown on a minimal medium.

H. J. Bensted

Noyes, H. E., McInturf, C. R. & Blahuta, G. J. **Studies on Distribution of *Escherichia coli* Endotoxin in Mice.** *Proc. Soc. Exper. Biol. & Med.* 1959, Jan., v. 100, No. 1, 65–8.

E. coli endotoxin was prepared from a strain isolated from a case of fatal human septicaemia. The endotoxin was then tagged with ^{51}Cr and was injected into mice by 3 routes—intravenous, intracerebral and intramuscular. When the first 2 were used, the endotoxin distribution patterns were similar for both routes—the endotoxin disappeared rapidly from the site of injection and was found largely in the liver. This seemed to indicate that the lethal effects of the endotoxin would develop when the hepatic concentration rose beyond a threshold limit, but this hypothesis was found to be untrue when the intramuscular route of injection was used: here, up to 50% of the endotoxin remained at the site of injection, blood levels rose but liver concentration was low. Thus the lethal effects of the endotoxin for mice could not be related to one distribution pattern. When mice were premedicated with trypan blue, it was found that there was an increase in circulating endotoxin (intramuscular and intravenous routes). This last finding confirms that trypan blue produces an increased susceptibility to endotoxin, supposedly by blocking the reticulo-endothelial system.

John S. Stevenson

Wust, C. J. **Mucoid Enhancing Antibody in Homologous Antiserum for *Escherichia coli*.** *J. Bacteriology.* 1959, Apr., v. 77, No. 4, 452–60, 3 figs. [14 refs.]

"An increase in the proportion of stable mucoid colony variants was found after exposure of *Escherichia coli* strain K-12 to homologous rabbit antiserum. These variants, maintained for many subcultures on noncarbohydrate containing medium, displayed the mucoid characteristic only when inoculated onto appropriate agar at temperatures below 30 C. Selected mucoid isolates, when grown on nutrient agar devoid of carbohydrate, possessed a new antigen(s), produced illness and death in mice, and showed increased resistance to phagocytosis.

"The increase in the proportion of mucoid colonies was attributed to a thermolabile, non-dialyzable mucoid enhancing antibody which was unassociated with titratable agglutinins. The antibody could be removed by specific adsorption with K-12. Antisera prepared against antigenically related mutants of K-12 contained the antibody to a varying degree corresponding to the relative genetical distance of each strain from the parent."

Stadler, Joan & Yanofsky, C. **Studies on a Series of Tryptophan-Independent Strains derived from a Tryptophan-Requiring Mutant of *Escherichia coli*.** *Genetics.* 1959, Jan., v. 44, No. 1, 105–23, 3 figs. & 2 diagrams. [10 refs.]

Pitzurra, M. & Szybalski, W. **Formation and Multiplication of Spheroplasts of *Escherichia coli* in the Presence of Lithium Chloride.** *J. Bacteriology.* 1959, May, v. 77, No. 5, 614–20, 9 figs. [19 refs.]

Szybalski, W. & Pitzurra, M. **Mechanism of Chemical Mutagenesis. III. Induced Mutations in Spheroplasts of *Escherichia coli*.** *J. Bacteriology.* 1959, May, v. 77, No. 5, 621–2.

Horiuchi, T., Horiuchi, S. & Mizuno, D. **A Possible Negative Feedback Phenomenon controlling Formation of Alkaline Phosphomonoesterase in *Escherichia coli*.** [Correspondence.] *Nature.* 1959, May 30, v. 183, 1529–30, 2 figs.

Koch, A. L. & Vallee, G. **The Properties of Adenosine Deaminase and Adenosine Nucleoside Phosphorylase in Extracts of *Escherichia coli*.** *J. Biol. Chem.* 1959, May, v. 234, No. 5, 1213–18, 3 figs. [24 refs.]

Melnykovych, G. & Johansson, K. R. **Effects of Chlortetracycline on the Stability of Arginine Decarboxylase in *Escherichia coli*.** *J. Bacteriology.* 1959, May, v. 77, No. 5, 638–41, 3 figs.

MOROWITZ, H. J. **The Use of Hanging-Strip Electrophoresis to Study Statistical Constraints in the Amino Acid Order of** *Escherichia coli*. *Biochim. et Biophys. Acta.* 1959, June, v. 33, No. 2, 494–504, 4 figs.

MOROWITZ, H. J. & BARRA, R. V. **Statistical Constraints in the Order of Leucine and Isoleucine in the Protein of** *Escherichia coli*. *Biochim. et Biophys. Acta.* 1959, June, v. 33, No. 2, 505–8.

ŠKODA, J., KÁRA, J., ŠORMOVÁ, Z. & ŠORM, F. **Inhibition of** *Escherichia coli* **Polynucleotide Phosphorylase by 6-Azauridine Diphosphate.** *Biochim. et Biophys. Acta.* 1959, June, v. 33, No. 2, 579–80, 2 figs.

BARBOUR, R. G. H. **The Adsorption by** *Aerobacter aerogenes* **of** *p*-**Hydroxybenzoic Acid and its Esters and of Sodium Benzoate at Different pH Levels.** *Australian J. Biol. Sci.* 1959, May, v. 12, No. 2, 204–12, 4 figs.

COETZEE, J. N. **Some Properties of a Morphological Variant of a Strain of Proteus Vulgaris.** *South African J. Lab. & Clin. Med.* 1959, Mar., v. 5, No. 1, 16–28, 8 figs. [17 refs.]

"Stock cultures of a proteus strain were found to consist of 3 distinct colonial variants X, Y and Z. One of these (X) has many of the features of an 'R' variant. This type X was found to occur in cultures initiated with single Y or Z cells that had been submitted to very heavy and prolonged population pressure. Nutrient agar also apparently favours the establishment of this type. These are the only conditions under which X types are detectable, and fluctuation experiments to test the possibility of X colonies arising by a process of mutation from Y or Z varients have not yet been devised. Possible reasons for this failure are mentioned. Under conditions of continuous logarithmic growth, initially pure X cultures (originating from Y or Z types) are entirely replaced by the Y type. A fluctuation experiment was designed which supported the mutational hypothesis for the origin of Ys from Xs. This mutation rate, calculated from long-term continuous culture experiments, proved to be $5{\cdot}3 \times 10^{-3}$/bacterium/generation."

MCCORQUODALE, D. J. & ZILLIG, W. Untersuchungen zur Biosynthese der Proteine, II. Über die Verteilung der aminosäureaktivierenden Enzyme in Zellfraktionen aus Homogenaten von *Escherichia coli* B. **[Studies on the Biosynthesis of Proteins. II. Distribution of the Amino Acid Activating Enzyme in Cell Fractions of Homogenates of** *Escherichia coli* **B]** *Hoppe-Seyler's Ztschr. physiol. Chem.* 1959, v. 315, Nos. 1/3, 86–9.

HALL, H. E. & HUMPHRIES, J. C. **The Relationship between Insusceptibility to Phagocytosis and Virulence of Certain** *Klebsiella pneumoniae* **Strains.** *J. Infect. Dis.* 1958, Sept.–Oct., v. 103, No. 2, 157–62. [20 refs.]

The authors examined the relationship between virulence and insusceptibility to phagocytosis with 4 strains of *Klebsiella pneumoniae* (Julianelle type A). 3 of the strains 69M, 108M, and ScM were capsulated and showed differences in virulence for mice, the LD50 titres being for strain 69M, $2{\cdot}0 \times 10^2$ bacteria; strain 108M, $4{\cdot}1 \times 10^4$ bacteria; strain ScM, $5{\cdot}6 \times 10^7$ bacteria. These titres were identical at the start and finish of the experiments. The fourth strain 108S—unencapsulated and avirulent; LD50 $3{\cdot}9 \times 10^8$ bacteria—was an S state variant of strain 108M. With the following optimum conditions: ratio of bacteria to phagocytes (mouse) 50 : 1 in 20% serum incubated at 37°C. for 30 minutes, it was found that the avirulent S state strain 108S was highly susceptible to phagocytosis, organisms being observed in all the phagocytes. The most virulent strain 69M was very resistant, being found in only 4% of the phagocytes and the intermediate virulent strains 108M and ScM were present respectively in 22% and 79% of the phagocytes. There thus was a correlation between virulence and insusceptibility to phagocytosis. Virulence cannot be explained on the basis of capsule size alone, as although the capsule of strain 108M was thinner than that of the insusceptible virulent strain 69M the capsule of the very susceptible strain ScM was just as thick. *Elizabeth M. Harper*

EPSTEIN, S. S. & PAYNE, P. M. **The Effect of Some Variables on Experimental** *Klebsiella* **Infections in Mice.** *J. Hygiene.* 1959, Mar., v. 57, No. 1, 68–80, 5 figs. [13 refs.]

9 strains of various *Klebsiella* species (2 were not capsulated) were inoculated into groups of 10 mice. The variables tested were dose, age of culture, route of inoculation (oral or intraperitoneal), weight of mice, and the effect of repeated subculture.

From the results the authors found that 7 strains were more virulent when given by mouth than by intraperitoneal inoculation; that 16-hour cultures were more virulent than older cultures, and capsulated more virulent than non-capsulated. 20 subcultures did not affect the virulence of the one strain tested. [5 of the 9 strains were classical and had been in the National Collection of Type Cultures for more than 20 years.] *S. T. Cowan*

GROMAN, N. B. & MEMMER, Ramona. **Lysogeny and Conversion in Mitis and Mitis-Like** *Corynebacterium diphtheriae*. *J. General Microbiol.* 1958, Dec., v. 19, No. 3, 634–44. [14 refs.]

Colonies of toxigenic *mitis* and *mitis*-like corynebacteriae isolated in the Western United States and Canada were examined in respect of their capacity for lysogeny and the capacity of their bacteriophages to convert non-toxigenic to toxigenic strains. The criteria

adopted for accepting those strains as *mitis* or *mitis*-like were that they should produce acid from glucose and maltose but not from sucrose, glycogen or starch and that they were devoid of urease and did not reduce nitrate to nitrite (there was one exception to the last feature). Their morphology corresponded to that characteristic of this group but haemolysin production and colonial morphology were more varied. Notwithstanding minor variations, the large size, convex contour and glistening appearance of the colonies, justify their description as *mitis* or *mitis*-like rather than *gravis* or *intermedius* strains.

Using well established methods for the preparation of bacteriophages and testing these against a number of standard indicator strains and also against all the other strains in the group examined, the authors were able to demonstrate lysogeny in 25, *i.e.* 46% of these strains and they point out that the capacity for lysogenesis could probably be demonstrated in a larger number if a wider group of indicator strains were used. With the exception of 4 strains all the bacteriophages isolated were active against all of the group of indicator strains used. The reactions of the strains to certain bacteriophages already in possession of the authors, *i.e.* the temperate bacteriophages β and γ and a B phage which is a virulent mutant of β, have been examined and the interrelationship between these phages and those which they isolated from bacteria have been investigated. The capacity of antiserum to the phage γ to neutralize the action of these various phages suggests a close relationship. Further lysogenic strains were obtained from a streptomycin-resistant strain, C4, and the sensitivity of each of these derived strains to the phages carried by each of the other derived strains was investigated. It was shown that the phages isolated from any one of these strains immunizes the host culture against all the other phages derived from these strains.

The general effect of all this is to suggest a close antigenic resemblance between a considerable group of *mitis* strains derived from different areas, which does not fall into line with the diversity of these strains shown by the methods of agglutination as usually performed [There is a marked divergence between the results recorded above and those of CHRISTENSEN, who found that lysogenic *gravis* strains only produced phages active against *gravis* strains falling in the same immunological group, as determined by sensitivity to agglutinating sera (this *Bulletin*, 1958, v. 33, 265).]

J. W. McLeod

BEN-EFRAIM, S. & LONG, D. A. **The Sensitising Power of Diphtheria Prophylactics in relation to Poliomyelitis.** *Lancet.* 1957, Nov. 23, 1033–5, 2 figs. [11 refs.]

Guineapigs injected intramuscularly in the leg with various diphtheria prophylactics were tested 28 days later for their sensitivity to diphtheria toxoid, measured by the area of inflammation 24 hours after intradermal inoculation. Single injections of formol toxoid (FT) or of toxoid-antitoxin floccules (TAF) did not induce significant sensitivity, but the adsorbed antigens, alum-precipitated diphtheria toxoid (APT) and aluminium-phosphate-precipitated diphtheria toxoid (PTAP) induced striking hypersensitivity, PTAP more so than APT. The addition of pertussis vaccine to FT increases hypersensitivity to the maximal level induced by the aluminium-phosphate-precipitated toxoid. The authors draw attention to the correlation between sensitizing power of these prophylactics and their ability to cause provocation poliomyelitis in man, the Medical Research Council study [this *Bulletin*, 1957, v. 32, 233] having shown that the greatest risk was associated with alum-precipitated mixed diphtheria-pertussis prophylactic, and least with FT.

J. Knowelden

CALALB, G., POENARU, Elena, STĂNICĂ, Ecaterina, SARAGEA, Alice, KRANZDORF, H., MAXIMESCO, Paula, ESRIG, Mira & STOIAN, Cecilia. Le vaccin associé diphtéro-tétanique. I. [**The Associated Diphtheria-Tetanus Toxoid**] *Arch. Roumaines Path. Expér. et Microbiol.* 1958, Sept.–Dec., v. 17, Nos. 3/4, 545–51. [21 refs.]

The English summary appended to the paper is as follows:—

"The association of diphtheria and tetanus toxoid, their purification and adsorption on PO_4Al, results in synergic effects as regards their immunizing activity and by no means in competition. These statements are valid only in the case of an adequate dosage of the two associated antigens.

"In order to provide for a satisfactory production of bi-toxoid prophylactic the batches of diphtheria and tetanus toxoid used should possess high antigenic values and be as homogeneous as possible in every respect, from one batch to another."

KWAPINSKI, J. Badanią nad budową antygenową drobnoustrojów rzedu *Actinomycetales*. *III*. Pokrewieństwo antygenowe szczepów rodzaju *Corynebacterium* i *Mycobacterium*. [**Studies on the Antigenic Structure of** *Actinomycetales*. **III. Antigenic Relationship between** *Corynebacterium* **and** *Mycobacterium* **Strains**] *Archiwum Immunol. i Terapii Dośw.* Warsaw. 1958, v. 6, No. 1, 29–62, 22 figs. [23 refs.] English summary.

A comparative examination has been made of fractions obtained from *Mycobacterium tuberculosis* var.-*hominis*, *Myco. phlei*, *Corynebacterium diphtheriae* and *C. hofmanni* by chemical procedures developed by the author, involving extraction with lipid solvents, dilute acetic acid and increasing concentrations of sodium hydroxide. The sugars present in the polysaccharide fraction and the amino-acids present in the protein fraction were identified by chromatography, and the results are given in detail in tables together with the results of determinations of total nitrogen and phosphorus and reducing substances. Some differences were found in the composition of fractions obtained from the different organisms, and the 2 pathogens contained 2 unidentified amino-acids. The lipid fraction of *C. diphtheriae* contained 2 unidentified fatty acids. Antigenic relationships were observed in cross-fixation tests between the protein and lipid fractions obtained from

the 2 genera. [The paper contains much experimental detail and should be consulted in the original for further information.] *D. J. Bauer*

SAXHOLM, R. **An Experimental Investigation of Methods for the Cultivation of** *Mycobacterium tuberculosis* **from Sputum.** *Acta Path. et Microb. Scandinavica.* 1958, Suppl., 126, pp. vi + 148. [Numerous refs.]

The introduction to this monograph is a comprehensive review of the various agents that have been used since 1892 for excluding unwanted bacteria from cultures of the tubercle bacillus, and most readers will feel that the last word on this subject must have already been written. The author, however, then presents 133 pages describing investigations into the use of cationic quaternary ammonium salts (Quat) for this purpose.

Although these investigations are mostly concerned with a mucolytic-enzyme-Quat method, the possibility of replacing the enzyme or the Quat by adjustment of *p*H to make either the Quat mucolytic or the enzyme bactericidal is also explored.

Some preliminary experiments with pancreatin, papain, lysozyme, hyaluronidase, streptokinase-streptodornase, an enzyme from *Streptomyces albus* as mucolytic agents, and glycerol, ethylene glycol, propylene glycol and 13 various Quats as antibacterial agents gave results that encouraged the further experiments with pancreatin and the Quats. These further experiments were planned statistically, on a factorial basis, so that the effects of varying more than 1 factor in the same experiment could be determined; the investigations were also designed so that the value of the enzyme-Quat method could be compared with the sodium hydroxide method.

The experiments were made on specimens of positive sputum to which tubercle bacilli were added, and the results, which are presented in 54 tables, are extensively discussed. The following account summarizes the author's conclusions.

1% pancreatin, the concentration mostly used in the experiments, homogenized a little better than 0·25%, but the differences observed with concentrations ranging from 0·25 to 2% were small.

The concentration of Desogen$_L$ (methylphenyl-dodecyl-trimethyl-ammonium methosulphate) recommended is 1–2%, and although the yield of tubercle bacilli is not very different over a wide range of concentrations, a statistically significant improvement in decontamination was observed between 0·25 and 5%.

Between 4–37°C., the range of temperatures tested, adequate mucolysis occurred, but the yield of tubercle bacilli was slightly greater at the lower temperatures and the contamination rate decreased slightly as the temperature rose from room temperature to 37°C., although it was also a little lower at 4°C. than at room temperature.

Although the most convenient period of exposure would appear to be 24 hours at 4°C. or either 4 hours or 19–24 hours at room temperature, no marked reduction in the yield of tubercle bacilli was noted until after 6 days' exposure; a slight decrease was, however, detected from the second day onwards.

There was a slight reduction in the enzyme activity of the pancreatin-Desogen$_L$ mixture on storage at room temperature, but the activity was still adequate after 7 months. Use of either an alkaline borate or phosphate buffer up to *p*H 9·0 slightly increased the mucolytic action of the mixture.

Equal volumes of sputum and digestion mixtures are recommended and, although there was no significant difference in the yield of tubercle bacilli from 0·5 ml. and 3 ml. volumes of sputum, the contamination rate was higher with the larger volume. The contamination rate was also lower when the inoculum consisted of 1 drop of the mixture instead of 10 drops, but the yield of tubercle bacilli was less. The larger inoculum, however, caused some softening of the egg medium.

The most promising Quats besides Desogen$_L$ were Vantoc B (alkyl pyridinium halide, essentially tetradecyl pyridinium bromide), Bradosol (β-phenoxyethyl-dimethyl-dodecyl-ammonium bromide), and Ceatavlon (cetyl - trimethyl - ammonium bromide). The solid Desogen$_S$ (dodecanoyl-N'-methyl-aminoethyl-(phenyl-carbamyl-methyl)-dimethyl-ammonium chloride) was less effective than the liquid Desogen$_L$. Vantoc B might be more effective than Desogen$_L$, but confirmation is required from more experiments.

Of the mucolytic action of the other enzymes examined, papain appeared to be somewhat less than that of pancreatin, but otherwise it yielded comparable results; pepsin necessitates a low *p*H, but it appears to be satisfactory, although more investigations are needed to be certain of this.

The sodium hydroxide and the pancreatin Desogen methods were compared in 6 experiments on 6,342 specimens. In each of these experiments a greater yield of tubercle bacilli and earlier growth were obtained by the enzyme method, the difference in yield being statistically significant in 2; the contamination rate was, however, less with the sodium hydroxide method. [The sodium hydroxide method consisted of adding 2 volumes of 4% sodium hydroxide to 1 volume of the specimen, shaking and incubating the mixture for 20 minutes at 37°C. After centrifuging, the deposit was neutralized with hydrochloric acid and an inoculum of 3 drops placed on the medium.]

Löwenstein-Jensen and Tarshis blood agar media, but not Tween-albumin medium, are satisfactory for use with this pancreatin-Desogen method, but the size of the container had some effect. A higher yield of positive cultures was obtained when 1 oz. Universal containers were used instead of 13 × 95 mm. tubes. Whether a cork or rubber stopper was used did not affect the yield of tubercle bacilli but the contamination rate was slightly higher with the cork stoppers.

In guineapigs a greater number of specimens were shown to contain tubercle bacilli when the animals were inoculated with specimens untreated than when treated with sodium hydroxide, but the mortality rate was insignificantly higher. Treatment with pancreatin-Desogen yielded slightly more positive results than treatment with sodium hydroxide. The guineapig method was superior to any of the cultural methods for detecting tubercle bacilli.

No acid-fast saprophytes were isolated during the investigation.

The mixture finally recommended consists of equal parts of 2% pancreatin solution, Seitz filtered, and 3% Desogen$_L$, both dissolved in Clark and Lubs borate buffer *p*H 9·0. [The author emphasizes that the Desogen was not the commercial liquid, as this contains a perfume and was less effective; the pure substance was supplied by the manufacturers (Geigy).] The pancreatin may be reduced to give a final concentration of 0·25%, depending partly on the sample used.

The procedure recommended consists of adding an equal part of the mixture to the sputum, and after a brief shaking by hand, leaving the receptacle in a dark cupboard for 4–24 hours, or in the refrigerator for a longer period. The medium should be inoculated directly with the mixture, without centrifuging or neutralization, and incubated with its surface horizontal. The number of manipulations are therefore very few and the risks to the operator are thus reduced to a minimum.

S. R. M. Bushby

AOYAGI, T. & MIZUNO, D. **Cultivation of Mycobacteria rocked in Non-Protein Medium containing a High Concentration of Tween 80.** *J. General Microbiol.* 1959, Apr., v. 20, No. 2, 173–9, 6 figs. [18 refs.]

This paper deals with the growth of 3 strains of *Mycobacterium tuberculosis* (H37Rv, H2 and an avirulent strain), BCG, *Myco. avium, Myco. phlei* and *Myco. smegmatis* in a defined medium containing a high concentration of Tween 80 but no albumin fraction V. Heavy inocula, to give 0·3–0·5 mgm. per 10 ml., were used and the cultures were made in ⊥ tubes, 26 cm. long × 1·8 cm. external diameter with the inlet side arm 4 cm. long. These tubes were rocked 30 times per minute in a water-bath at 37°C., and the amount of growth was estimated photometrically at various intervals. The shape of the culture tube enabled these readings to be made simply by placing the tube directly into the absorptiometer, and it also avoided excessive aeration during the rocking. The bacillary growth appeared macroscopically to be uniform but approximately only one-third of the bacilli were single organisms, the rest being present in clumps of 2 to 20 bacilli.

The basic medium, which was essentially that of Sauton, consisted of 4·0 gm. asparagine or sodium glutamate, 2·0 gm. citric acid, 0·5 gm. K_2HPO_4, 0·5 gm. $MgSO_4.7H_2O$, 0·05 gm. ferric ammonium citrate and 60 ml. glycerol dissolved in 980 ml. distilled water or 20 gm. glucose. With the medium containing asparagine and glycerol, all the strains showed increase in growth during the incubation period of 150 hours as the concentration of Tween was increased from 0·05 to 1·0%, and further increases of up to 3·0% did not produce any greater increase in growth; with glutamate as the source of nitrogen the optimum concentration of Tween was 0·7–1·0%.

Calculations of the generation times of each of the organisms showed that asparagine and glucose rather than glutamate and glycerol were the preferred sources of nitrogen and carbon. The optimum concentration of asparagine or glutamate, in the presence of glucose, was about $10^{-2·5}$M, and although reducing the concentrations to 10^{-4}M did not greatly affect the growth, increasing the concentrations diminished the growth; $10^{-0·5}$M glutamate almost abolished the growth.

All the strains were successfully subcultured in the logarithmic phase more than 3 times in the medium with inocula of 0·5 ml. per 10 ml. The avirulent human strain and *Myco. smegmatis* were subcultured 25 times in the asparagine-glucose medium and although the smegma bacillus showed a marked decrease in acid fastness after the 10th passage, the tubercle bacillus showed only a slight reduction after the 20th passage. Neither organism showed any change in generation time during these passages, and no morphological changes were detected in electron photomicrographs of the tubercle bacillus taken at the 10th and the 25th passages.

The fact that albumin was not essential for growth of these mycobacteria in the presence of the high concentration of Tween 80, which was known to contain 0·55% free acid as oleic acid, was assumed to be due to the large inoculus used. *S. R. M. Bushby*

AOYAGI, T. & MIZUNO, D. **A Rapid Antibacterial Test for Mycobacteria using a Reverse T Type of Tube in Rocked Culture.** *J. General Microbiol.* 1959, Apr., v. 20, No. 2, 180–83, 1 fig.

Using the method described in the previous paper [above] for determining the growth rate of tubercle bacilli, the authors have measured the sensitivity of H37Rv and a strain of *Mycobacterium avium* for a number of antituberculous drugs.

The percentage inhibition of growth produced by 2 or 3 concentrations of the drugs was plotted on probit-log paper and the concentration which produced 50% inhibition was accepted as a measure of the sensitivity of the strain. The bacilli used for the inoculum were in the logarithmic phase of growth and these 50% inhibition doses of the drugs could be determined after 48 hours' incubation for the human strain and 8 hours for the avian strain.

The sensitivity figures reported by the authors are not compared with those obtained by the more usual methods but they are of the same order. 2 defects for the method are said to be that the determination of the optical density in the presence of a coloured drug makes the method rather tedious, and that the high concentration of Tween 80 (1%) used in the Sauton medium may affect the activity of the drugs.

S. R. M. Bushby

WAYNE, L. G. **Quantitative Aspects of Neutral Red Reactions of Typical and "Atypical" Mycobacteria.** *Amer. Rev. Tuberculosis.* 1959, Apr., v. 79, No. 4, 526–30, 1 fig.

In the neutral red test of Dubos and Middlebrook methanol-washed mycobacteria are treated with the dye in *p*H 9·5 buffer, and in the micro-colonial test of Wayne [this *Bulletin*, 1955, v. 30, 1106], the bacilli are grown on a Millipore membrane, stained *in situ* with acidified alcoholic neutral red solution and then treated

with the alkaline buffer. Although virulent bacilli stain red by both methods, the atypical mycobacteria do not always behave the same in both methods; by the Dubos and Middlebrook technique photochromogens are generally positive, but the non-photochromogens and the skotochromogens are very variable, whereas by the micro-colonial method all these atypical bacilli are uniformly positive. The experiments described in this paper were undertaken in an attempt to explain the discrepancies and they were made on a variety of mycobacteria.

A modification of the Dubos and Middlebrook technique was used in which the intensity of staining was compared by means of colour standards, before and after rewashing the bacilli in the alkaline buffer. An equivalent of the micro-colonial test was attained by pre-staining suspensions of the bacilli with an acidified saturated ethanol solution of neutral red and then washing them first with water and then in buffer solution of a desired *p*H.

The results with the Dubos and Middlebrook stain showed that even saprophytes absorb significant amounts of dye and that even from virulent tubercle bacilli treatment with the buffer solution elutes some of the absorbed dye. The alkali apparently not only interferes with absorption of the dye but also affects the tint of the dye.

By the pre-staining technique the mycobacteria could be divided into groups depending upon the degree of retention of the dye when the bacilli were suspended in buffers of increasingly alkaline *p*H and on the time required for fading; *Mycobacterium tuberculosis* was the most resistant, followed, in order, by: the photochromogens; *Myco. avium*, the Battey types of atypical mycobacteria and the skotochromogens; the saprophytes, *Myco. fortuitum* and the nocardiae. A small group of non-photochromogens strongly resisted decolourization at *p*H 10·5 for 24 hours but *Myco. fortuitum* and the nocardiae decolourized after only a few seconds' exposure. Whether the differences are due to a quantitative or qualitative dye-binding component in the bacilli is not yet decided. *S. R. M. Bushby*

KATSUYAMA, S. & KANAI, K. **Comparative Studies on the Virulence of Two Substrains (H2Rv and H2Ra) dissociated from a Strain of Virulent Tubercle Bacilli (H2) by Single Cell Cultivation.** *Japanese J. Med. Sci. & Biol.* 1958, Oct., v. 11, No. 5, 307–15, 5 figs.

These 2 sub-strains, H2Rv and H2Ra, were isolated by micromanipulation as single cell cultures from a human type of virulent tubercle bacilli, H2, [this *Bulletin*, 1959, v. 34, 659 *bis*] and in the experiments reported in this paper, their virulences were compared with those of H37Ra, BCG and H2.

In the first experiment, groups of 17, 17 and 18 guineapigs were infected intravenously with H2Ra, H37Ra and H2Rv, respectively. On the day of infection and weekly, 2 to 4 animals of each group were killed and viable counts made on homogenates of the spleens. The counts show that H2Ra and H37Ra behave similarly for H2Ra multiplied during the first 2 weeks and then rapidly decreased in number, H37Ra multiplied less during the first week, kept level for the next 2 weeks and then decreased rapidly in number. In contrast, H2Rv, multiplied 1,000-fold during the first 2 weeks and then remained at this level for the next 4 weeks. The changes in the weights of the spleens supported these differences in virulence.

In the second experiment, 3 groups for 5 guineapigs were infected subcutaneously with 16×10^6 v.u. (viable units) of H2Ra, 19×10^6 v.u. of H2Rv and 21×10^6 v.u. of a culture of H2Ra which had been passaged through a guineapig and recovered from the spleen; 6 weeks later the animals were killed and examined. The animals infected with the H2Rv had innumerable tubercles in the liver, spleen and less often, in the lungs, and generalized swelling of the lymph glands. In contrast, the animals infected with the other 2 strains were almost devoid of visceral lesions, the only constant finding being swelling of the draining lymph node.

In the third experiment, in which groups of 10 guineapigs were infected intracerebrally with approximately 20×10^5 v.u. of H2Rv and H2Ra, the animals infected with H2Rv lost weight, 9 became paralysed within 25 days and all died during 21–40 days after infection. In contrast, the animals infected with H37Ra gained weight, and only 2 died in 40–63 days, the others surviving 74 days.

In the fourth experiment, groups of 10 guineapigs were vaccinated with 2×10^6 v.u. of BCG, 9×10^6 v.u. of H37Ra and 7×10^6 v.u. of H2Ra. 3 weeks later the animals were tested with tuberculin and after a further 3 weeks the animals were challenged with 5×10^4 v.u. of a mutant of H37Rv resistant to streptomycin. Judged by the bacillary multiplication of the challenge strain and the degree of tuberculous involvement, H2Ra has the same grade of immunogenicity as BCG and H37Ra.

In the fifth experiment, H2, H2Rv and H2Ra were shown to be of equal sensitivity *in vitro* to streptomycin, isoniazid, PAS and kanamycin.

In discussing these results, the authors emphasize that the difference in the virulence of these 2 sub-strains was most strikingly revealed by subcutaneous injection and although the difference could be attributed to differences in invasiveness, the fact that both H2Ra and H37Ra show initial multiplication in the animals suggests that the difference is due to these strains being more susceptible than H2Rv to the acquired resistance that the animal develops during the infection.

The fact that H2Ra was still avirulent after passage through a guineapig suggests that the sub-strain is homogeneous and stable in its virulence.

S. R. M. Bushby

KANAI, K., KATSUYAMA, S., NAKAJIMA, M., MAEDA, T. & MARUYAMA, Y. **Some Aspects of Bacterial Mutation from Streptomycin Dependence to Nondependence in a Strain of Tubercle Bacilli.** *Japanese J. Med. Sci & Biol.* 1958, Aug., v. 11, No. 4, 235–49. [22 refs.]

KANAI, K., MARUYAMA, Y., KATSUYAMA, S. & MAEDA, T. **Further Analysis of Bacterial Mutation from Streptomycin Dependence to Nondependence in a Strain of Tubercle Bacilli, particularly in association with Acriflavine Resistance.** *Japanese J. Med. Sci. & Biol.* 1958, Aug., v. 11, No. 4, 251–8.

LYON, R. H. & HALL, W. H. **The Effect of Isoniazid upon the Growth of Tubercle Bacilli from Pulmonary Lesions.** *Amer. Rev. Tuberculosis.* 1959, Apr., v. 79, No. 4, 518–21. [Refs. in footnotes.]

These investigations were made on 73 lesions from resection specimens of 65 patients who had been treated with streptomycin and PAS, or with isoniazid and PAS or streptomycin. Nodules from 3 patients who had had no chemotherapy were also included. The lesions were homogenized and suspended in Dubos medium, without Tween but containing 25 units penicillin per ml. These suspensions were centrifuged and the supernatant fluid was incubated and the sediments were inoculated into 3 tubes of Löwenstein-Jensen medium and into 2 guineapigs. The cultures were then incubated for up to 9 months. Stained smears and sections were also examined for acid-fast bacilli.

AUERBACH *et al.* [this *Bulletin*, 1956, v. 31, 263], reporting from the results of a similar study, claimed that tubercle bacilli often survived in closed necrotic lesions but took much longer than usual to grow. The present study showed that tubercle bacilli were recovered from only 21% of 52 unsloughed nodular lesions, 48 of them being from 40 patients who had had only 1 course of chemotherapy; Auerbach *et al.* recovered tubercle bacilli from 78% of similar lesions.

Tubercle bacilli were grown from 27% of the active lesions and from only 12% of those showing intermediate healing. Attainment of D'ESOPO'S target, *i.e.* negative sputum, cavities closed and maximum radiographic clearing, did not assure healing, for 23 of 37 nodules in such cases were microscopically judged as active, and tubercle bacilli were recovered from 16%. Evidence of healing was most frequently seen in these lesions when they were from patients treated with isoniazid.

The effect of the duration of the preoperative chemotherapy was studied on 52 nodular lesions, 37 of which were from target-point patients; tubercle bacilli were recovered from 3 of 7 target-point patients who had been treated with 1 gm. streptomycin, twice weekly, and 12 gm. PAS daily for 8 or more months, but from none of 7 similar patients treated with 300 mgm. isoniazid daily for 8 or more months. There was no significant difference in the recovery of bacilli from nodules in this type of patient treated either 0–7 months or 8 or more months. Even in patients treated with isoniazid, acid-fast bacilli were commonly seen in unsloughed nodular lesions.

Acid-fast bacilli were detected microscopically in 64 of the 76 lesions, and although they were found more often in the sections, there was no difference when lesions were positive by culture.

As tubercle bacilli were grown from only 15% of lesions from the isoniazid-treated patients compared with 36% from the streptomycin-PAS treated patients, the authors suggest that isoniazid sterilizes and leads to earlier healing.

Although it was only in re-treated patients that there was any evidence that prolonged incubation of the cultures leads to a greater incidence of positive culture, the authors maintain that a minimum of 2 months' incubation is essential. They observed no significant difference in the incidence of recoverable bacilli by culture and guineapig inoculation. *S. R. M. Bushby*

VIALLIER, J., OLLAGNIER, C. & AUGAGNEUR, J. Recherches sul l'activité antituberculeuse du crotonaldéhyde isoniazide. [**Investigation into the Antitubercular Activity of the Crotonaldehyde of Isoniazid**] *C.R. Soc. Biol.* 1959, v. 153, No. 1, 109–10.

Grown in Youmans medium plus horse serum, 12 recently isolated strains of tubercle bacilli, sensitive to less than 0·1 μgm. isoniazid per ml., were also similarly sensitive to the crotonaldehyde of isoniazid, and although 7 strains resistant to 20 μgm. isoniazid per ml. were also resistant to the molecular equivalent of this aldehyde, when 9 isoniazid-resistant strains were tested against a range of concentrations equivalent to 20–60 μgm. isoniazid per ml., 6 were found to be less resistant to the aldehyde. The examination of 39 strains isolated from patients during treatment with the aldehyde confirmed these results, for whereas strains sensitive to isoniazid were equally sensitive to the aldehyde, a few of the isoniazid-resistant strains were rather less resistant to the aldehyde.

6 atypical mycobacteria were tested against the aldehyde and showed the same sensitivity as to the parent drug.

Determination of the tuberculostatic activity of the serum of patients undergoing treatment with 100 mgm. of the aldehyde per day showed that the peak absorption occurred 2–3 hours after dosing and that significant concentrations of the drug were still present at the 11th hour. Similar examinations of the urine showed that most of the drug is excreted within 24 hours. These specimens showed no activity against an isoniazid-resistant strain. *S. R. M. Bushby*

ZSOLNAI, T. Versuche zur Entdeckung neuer Tuberkulostatika. VI. Einige neuere Derivate des Isonikotinsäure-hydrazids. [**Search for New Tuberculostatics. VI. Some Newer Derivatives of Isonicotinic Acid Hydrazide**] *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 175, Nos. 3/4, 269–81. [34 refs.]

The English summary appended to the paper is as follows:—

"The author produced some new derivatives of isonicotinic acid hydrazide and tested their tuberculostatic activity in vitro. The correlations between the chemical structure of the different compounds and their tuberculostatic activity are discussed. From the results the

following conclusion is drawn: Only those isonicotinic acid hydrazide compounds are active in which

is present in an active state."

HIRANO, N., SUSHIDA, K. & YAMADA, S. **Chemotherapy of Tuberculosis. Antituberculous Activity of Isonicotinoyl-3.4-Diethoxybenzal Hydrazone (No. 284).** *Yokohama Med. Bull.* 1959, Feb., v. 10, No. 1, 20–26. [12 refs.]

In a previous paper [*Trop. Dis. Bull.*, 1959, v. 56, 56] the authors reported that isonicotinoyl-3,4-diethozybenzal hydrazone (No. 284) has a highly suppressive effect on experimental murine leprosy. In the present paper, the authors report the results of experiments in which they have compared the antituberculous activity of this drug with that of its dimethoxy analogue (Verazide) and isoniazid.

In the first 2 experiments, the comparison was made in mice infected intravenously with H37Rv and the activities were assessed by making viable counts on homogenates of the spleens and lungs of the infected animals. In the first experiment, the infecting dose was 48×10^4 viable units (v.u.) and the drugs were administered orally at 2·0 mgm. per day for 5 or 10 weeks; 7 days after the last dose the animals were killed. In the second experiment, the infecting dose was 45×10^4 v.u. and the daily dose of 284 was increased to 5 mgm. The results show that all 3 drugs were highly suppressive, the number of viable units per mgm. of tissue of the treated animals being from 0–25, with the majority of tissues containing less than 4 units per mgm., as compared with heavy uncountable growth from those of the untreated mice. The number of colonies suggested that 284 was almost as active as isoniazid after 5 weeks' treatment but somewhat less active after 10 weeks' treatment. Verazide was slightly but apparently definitely less active than 284.

In the third experiment, guineapigs were infected intracutaneously with 0·1 mgm. of H37Rv (23×10^4 v.u.) and 6 weeks later oral treatment with 20 mgm. 284 and 10 mgm. isoniazid 5 days a week was started; at this stage each of the animals had enlarged popliteal glands and skin lesions at the injection sites and 3 and 5 weeks later the animals were killed. The gross appearance of the lungs, liver, glands and the injection sites of the treated guineapigs showed that both drugs were highly active but the size of the glands and the number of lesions in the spleens and lungs suggested that 284 was more effective than isoniazid.

In the fourth experiment, in which mice were infected with tubercle bacilli resistant to isoniazid, neither 284, isoniazid nor isodiazol (5-(4-pyridyl)-1,3,4,oxadiazol-2-one) afforded any protection.

In view of the lower toxicity of 284, the authors consider it a more suitable agent than isoniazid for the treatment of human tuberculosis. *S. R. M. Bushby*

SIRSI, M. **Immunological Studies in Experimental Tuberculosis. Influence of Undernutrition on the Development of Resistance in B.C.G. Vaccinated Mice.** *J. Indian Med. Ass.* 1959, Mar. 16, v. 32, No. 6, 229–32, 1 fig.

This paper presents the results of deficient nutrition on the immunological response of mice to BCG vaccination.

Mice, 17–22 gm., were divided into 2 groups, 1 of which was kept on the standard diet and the other given 30% of their normal dietetic consumption for 3 weeks. This reduced intake was only sufficient for the animals to maintain their approximate weights. At the end of the period, half the mice of each group were vaccinated with 0·1 mgm. BCG intraperitoneally and 4 weeks later half of each of the sub-groups were inoculated with 0·1 mgm. H37Rv intravenously. All the animals were kept on their respective diets throughout the experiment and the effects of the diet on the immunity was judged by the median survival time of the various sub-groups, each of which consisted of 10 mice.

The median survival time of the animals on the standard diet was 37·2 days for the vaccinated-challenged group and 21·1 days for the challenged group, and for those on the restricted diet it was 57·5 for the vaccinated-challenged group and 17·8 for those challenged but not vaccinated. BCG vaccination alone had no adverse effect on mice either on the adequate or the deficient diet.

This experiment therefore indicates that the immunity conferred by BCG in underfed mice is in no way inferior to that conferred in well-fed animals.

S. R. M. Bushby

CONGE, G., COLLIN, E., LEVY, F. M. & DUBOS, R. J. **Microscopic Enumeration of Mycobacteria in Pulmonary Lesions of Tuberculous Mice. Effect of Prior BCG Vaccination.** *Amer. Rev. Tuberculosis.* 1959, Apr., v. 79, No. 4, 484–91, 4 figs. [16 refs.]

This paper is primarily concerned with the description and not the application of this method of measuring the protection afforded to mice by immunizing agents. In the experiments described, the left lung was fixed in Bouin's fluid and after embedding in paraffin, it was sectioned at 5μ thicknesses along a horizontal plane corresponding to the verticofrontal orientation in man; each section thus included both the apex and the other lobe. They were stained with carbol fuchsin and counterstained with malachite green and, although the whole lung was sectioned, only each 20th section was examined. [In a foot-note the authors state that more recently they have examined only each 80th section.] By this procedure with the sections numbered, it was possible to have an accurate picture of the anatomical location of each lesion, and a minimum of 10 lesions was examined for each lung.

The estimate of the number of organisms per lesion was based on those present in one section of the lesion, and the infecting dose was so arranged that the number present in each lesion was not too many for a direct enumeration; in practice this dose was $0·2 \times 10^{-3}$ dilution of an 8-day-old Dubos culture of H37Rv. In the

experiments described in this paper, the number of organisms in the lesions was also compared with the number of viable units grown from a homogenate of right lung.

In these experiments, BCG was injected intravenously into groups of 4-week-old mice and 3 weeks later the animals were challenged by the same route; some mice were killed 3 or 6 weeks after challenge for sectioning and the others were kept in order to determine the effect of the vaccination on the survival time. Under the conditions of these experiments it soon became apparent that vaccination did not reduce the number of lesions in the lungs although the number of bacilli were reduced 50-fold. The results also indicated (1) that a vaccine composed of 13-day-old bacilli gave a better protection than one of 20-day-old bacilli containing the same number of viable bacilli, and (2) that a lyophilization of a vaccine reduces its efficiency. These conclusions were the same whether they were based on the number of bacilli in the sections, the number of viable bacilli or the average survival time.

Incidentally, it was noted that as in other animals, the distribution of tuberculous lesions was not uniform, the lesions in the upper two-thirds of the dorsal area outnumbering those in the lower part.

The observation that the number of lesions is not affected by vaccination but that multiplication of the organisms is restricted after the lesions have become established, agrees with the observations of COHN *et al.* [this *Bulletin*, 1959, v. 34, 383] with air-borne infection, and it obviously has an important bearing on the mechanism of BCG immunity.

[The authors draw attention to the paper by SUTER and STRAIN (*ibid.*, 1959, v. 34, 572) describing a similar method to the one described here.] *S. R. M. Bushby*

BECK, A. **Atypical Acid-Fast Bacilli in Pulmonary Disease.** *J. Path. & Bact.* 1959, Apr., v. 77, No. 2, 615–24, 12 figs. on 3 pls. [33 refs.]

These cultures were recovered from sputa or laryngeal swabs since 1955 from 8 patients with pulmonary diseases and from the urine of 1 with a renal lesion. From 4 of the patients the bacilli were isolated on 3–7 occasions over periods of 2–18 months, and on no occasion were tubercle bacilli cultured from any of the patients except perhaps from the first patient. (From this patient tubercle bacilli were reported to have been grown, but at that time no attempt was made to identfy the cultures.)

In only 2 patients was the diseased lung examined. One of these patients had died and the lung showed extensive bilateral fibrocaseous disease with cavitation. There were no specific tuberculous histological changes, but numerous acid-fast bacilli were present in the lining of a cavity and these were isolated by culture. A left apical segment was obtained by resection from the second patient and, although the lesion was predominantly fibrocaseous with an occasional tubercle undergoing fibrosis, no acid-fast bacilli were seen; unfortunately this specimen was not cultured. In general, all these infections were of a chronic nature, and did not respond to chemotherapy.

Detailed cultural, biochemical and drug-sensitivity tests were made on the 9 strains and the same examinations were made for comparison on strains of human, bovine and avian tubercle bacilli, *Mycobacterium smegmatis*, *Myco. phlei* and *Myco. fortuitum*. The examination also included virulence tests, made by inoculating 20–100 million bacilli intravenously into mice and intracardially into guineapigs. Guineapigs were also tested intradermally with culture filtrates from 4 of the strains. The results are presented in 3 tables.

The length of the bacilli ranged from 2 to 6μ, and 6 of the strains showed marked barring. After prolonged cultivation, 3 of the strains became non-acid-fast and avirulent. All the strains gave a smooth yellow to orange growth which was fairly easily emulsified; they all grew at 37°C., but 4 also grew at 20°C. and 45°C., 2 grew at 20°C. but not at 45°C., and 3 grew at 45°C. but not at 20°C. All but 3 showed growth in glycerol-broth and in glycerol-agar. The majority grew much faster than tubercle bacilli, but 3 strains were slow growers.

Only 1 strain was strongly neutral-red positive but 4 were weakly positive; all were catalase-positive. Only 2 did not form aryl-sulphatase and both of these were neutral-red negative. 5 strains were resistant to isoniazid, streptomycin and PAS, but 3 others were sensitive to the 3 drugs and the other was resistant to isoniazid but sensitive to PAS and streptomycin.

3 of the strains produced lethal infections in the test animals; with these strains, the lungs of the mice were riddled with confluent nodules and they showed massive consolidation and necrosis with masses of bacilli but relatively little inflammatory reaction; less extensive lesions were also found in the liver, spleen and kidneys. The basic feature of the lesions in the guineapigs was a follicular proliferation of epithelioid cells without necrosis; giant-cells were rarely seen. In these animals the most extensive damage was seen in the spleen but the lungs, pericardium, lymph-glands, kidney and testis were also affected. As a rule, subcutaneous injection failed to produce progressive disease.

Guineapigs infected with 2 of the strains gave only doubtful skin reactions with the culture filtrates and although the animals infected with the other strains reacted to the antigens, the intensity of the reactions varied widely. Animals reacting to these antigens usually also reacted with a filtrate of *Myco. phlei* and 1 : 10 tuberculin, and, conversely, guineapigs infected with H37Rv also reacted to the antigens from the atypical mycobacteria.

Although the author finds it tempting to speculate on the pathological significance of these organisms, he suggests that they may have merely colonized tissues already damaged by earlier tuberculous infection.

S. R. M. Bushby

VIALLIER, J., CAYRÉ, R. M. & AUGAGNEUR, J. Sensibilité des mycobactéries atypiques aux différents antibiotiques. **[Sensitivity of Atypical Mycobacteria to Different Antibiotics]** *C.R. Soc. Biol.* 1959, v. 153, No. 1, 111–13.

These sensitivity tests were made on 6 strains of atypical mycobacteria isolated from sputum, gastric

washings or lung tissue. The medium used for the tests was that of Youmans containing horse serum.

The strains were insensitive to 100 μgm. PAS per ml., to 10 but not to 20 μgm. isoniazid per ml., to 25–50 μgm. cycloserine per ml. to 20–100 μgm. viomycin per ml. and 2 of the strains were inhibited by concentrations of 1–5 μgm. hydroxymycin per ml. and by 25 μgm. kanamycin per ml. Sensitivity to streptomycin increased during treatment with the drug from 20–100 μgm. per ml.

Mycostatin, penicillin and colimycin caused no inhibition at 25–50 μgm. per ml., and soframycin, ristocetin, novobiocin, oleandomycin, the tetracyclines and chloramphenicol caused only partial inhibition [presumably at 25–50 μgm. per ml.], whereas neomycin produced partial inhibition at 0·25 μgm. per ml. Erythromycin also showed partial inhibition but only with concentrations not easily obtained in man. *S. R. M. Bushby*

KÄPPLER, W. & IWAINSKY, H. Über Veränderungen in der Substratverwertung durch INH-resistente Mycobakterien (Myc. phlei). [**Changes in Substrate Utilization by** *Mycobacterium phlei* **Resistant to Isoniazid**] *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 174, Nos. 7/8, 506–13, 5 figs. [21 refs.]

BEKIERKUNST, A., SULITZEANU, D. & HALPERN, I. [**Cross Resistance in Experimental Tuberculosis and Brucellosis in Mice**] *Harefuah.* Jerusalem. (In Hebrew 261–4. [18 refs.] English summary 264.)

The English summary appended to the paper is as follows:—

"After vaccination with living or heat killed bacilli of Brucella 19 strain a resistance of mice to a challenge with virulent tubercle bacilli $H_{37}Rv$ was observed. Intraperitoneal vaccination of mice with living or dead BCG or acetone killed typhoid bacilli induced a resistance to a subsequent challenge with virulent Brucella bacilli. It was also found that in mice vaccinated with living or heat killed BCG or acetone killed typhoid bacilli, the distribution of acetone dried and radioiodinated Brucella bacilli injected into the mice was comparable to that found after previous vaccination with Brucella cells."

ALTENBERN, R. A., WILLIAMS, D. R. & GINOZA, H. S. **Effect of Cobalt on Population Changes in** *Brucella abortus*. *J. Bacteriology*. 1959, Apr., v. 77, No. 4, 509.

5 μgm. of cobaltous nitrate per ml. almost completely suppressed population changes of several smooth isolates of *Brucella abortus*, strain 19, in a defined medium, but significant suppression was seen in Albimi broth only at 20 μgm. cobalt per ml.

When smooth or derived non-smooth cells were grown in Albimi broth with 50 to 75 μgm. cobalt per ml. cyanide-sensitive respiration was significantly depressed, but cyanide-insensitive respiration was unchanged.

The results suggest a relation between population changes in cultures of *Brucella* and synthesis of haem enzymes involved in terminal oxidation.

H. J. O'D. Burke-Gaffney

MYERS, D. M. **Observations on a Chemical Test related to the Virulence of** *Staphylococcus aureus*. *Amer. J. Clin. Path.* 1959, Feb., v. 31, No. 2, 128–32.

An ammonium molybdate test (AMC) is described which the author claims is a better test for virulence of *Staph. aureus* than the coagulase or mannitol fermentation tests. 0·08 ml ammonium molybdate reagent (2·5 gm. q.s. to 100 ml. distilled water) is added to 4-hour cultures of the organism in human-plasma-saline medium. 0·04 ml. of a solution of 3 gm. sodium bisulphite and 1 gm. Pictol (p-methyl-aminophenol sulphate) in 100 ml. distilled water is added, followed by 0·2 ml. of 2% HCl. A blue colour due to reduction of the ammonium molybdate denotes a positive reaction.

This test applied to 156 strains designated *Staph. aureus*, from routine clinical material, showed no correlation with the coagulase or mannitol fermentation tests.

0·1 ml. of cultures of 20 strains was injected intraperitoneally into mice (1 mouse for each strain) and the recovery of organisms from spleen, liver or kidney from animals which died or were sacrificed at 7 days was taken to indicate virulence of the strain. Before injection 8 of 20 strains were AMC positive and virulent, 2 strains were AMC positive and non-virulent and 5 strains each were AMC positive and virulent and AMC positive and non-virulent. Strains did not always give the same reactions before and after passage.

9 of 45 strains from lesions classified by the author as local infections were AMC positive. 32 of them were coagulase positive. 24 of 24 strains said to come from "systemic infections" were AMC positive, 22 of them were coagulase positive.

The author states that this test detects an enzyme system or systems but this was not investigated, and he suggests that it is an indirect measurement of hyaluronidase production. *M. Patricia Jevons*

LIEBERMAN, Rose, DOUGLAS, J. O. A. & HUMPHREY, W., Jr. **Ascites induced in Mice by** *Staphylococcus*. *Science*. 1959, Mar. 20, v. 129, 775.

Mice were injected intraperitoneally with an antigen made from a recently isolated strain of *Staph. aureus* from an abscess. 16 mice were used in each group, one group received live vaccine, one group received heat-killed vaccine and one group received formolized vaccine. 2–3 injections were given at 5-day intervals and consisted of 0·3 ml. of a mixture of vaccine and Freund's complete adjuvant in equal parts.

Ascites (2–12 ml./mouse) appeared in 100% of mice in 1½–2 weeks where formolized or heat-killed organisms were used and in the 3rd or 4th week after live culture. Freund's adjuvant and broth alone produced ascites in 4/16 mice in 4 weeks.

Animals were killed after maximum ascites had been obtained and the serum and ascitic fluid was found by slide agglutination to contain an agglutinating antibody the titre of which varied between 1/2,000 and 1/4,000 [there is no note on the specificity of this antibody]. Similar results were obtained with an antigen made from a different strain of *Staph. aureus* combined with Freund's adjuvant without *Mycobacterium butyricum.* *M. Patricia Jevons*

D'Antona, D. L'anatossins stafilococcica in medicina umana. (Basi dottrinali, preparazione, controllo ed applicazioni pratiche.) [**Staphylococcal Toxoid in Human Medicine**] *Ann. Sclavo.* Siena. 1959, Jan.–Feb., v. 1, No. 1, 1–93, 6 figs. (4 coloured on 2 pls.) [707 refs.]

The English summary appended to the paper is as follows:—

"In the first part of this paper, the properties of staphylococcal toxin are described and their complex nature is indicated. The pathogenesis of staphylococcal infection is then examined as an expression of two clearly defined and separate factors, the first linked to the direct aggressive action of staphylococcal toxin, the other inherent in the appearance of sensitization phenomena to bacterial proteins, as demonstrated by means of intradermal reaction tests.

"Resistance to staphylococcal infection is expressed side by side by phenomena having a purely immunizing character, among which antitoxin is most significative, and by the setting up of a state of desensitization which facilitates mastery over the disease.

"Immunity and allergy can appear separately or can co-exist in the course of staphylococcal infection, but allergy seriously interferes with the initiation of immunity phenomena and with the elimination of the infective agent. Staphylococcal toxoid, both because of the immunity phenomena it produces, of which antitoxin is the specific manifestation, and because of the desensitizing phenomena prompted by its rational use, represents the most suitable remedy for the radical defeat of staphylococcal infection.

"In the second part of the paper, methods of preparation of staphylococcal toxoid are briefly reviewed; and this is followed by a particularized description of methods of controlling its safety and potency for the purposes of biological standardization.

"Finally, reasons are given for invalidating the immunizing efficacy of bacterial vaccines, in the form of bacterial emulsions used alone or associated with the anatoxin; and satisfactory results obtained following world-wide experience with staphylococcal toxoid in human medicine are reported, together with the practical methods of application which are most likely to assist its immunizing and desensitizing action."

Lowbury, E. J. L. & Hurst, L. **The Sensitivity of Staphylococci and other Wound Bacteria to Erythromycin, Oleandomycin, and Spiramycin.** *J. Clin. Path.* 1959, Mar., v. 12, No. 2, 163–9, 2 figs. [10 refs.]

This paper reports observations made principally with 620 strains of *Staphylococcus aureus* isolated from patients with burns in the Birmingham Accident Hospital. Sensitivity to erythromycin, oleandomycin and spiramycin was tested in ditch plates, 4 degrees of sensitivity or resistance being recognized. 267 strains fully sensitive to erythromycin were almost without exception fully sensitive to both other antibiotics. Of the remaining 353 strains showing different degrees of resistance to erythromycin, 36 were sensitive to oleandomycin, 211 were intermediate and 106 fully resistant when the plates were read at 18 hours, but these figures became 5, 59 and 289 when they were re-read at 42 hours: *i.e.* the effect of oleandomycin on many of these strains is only to delay growth. The behaviour of these and other types of strain was also followed by serial viable counts in broth cultures. 259 of the 353 erythromycin-resistant strains were sensitive to spiramycin: continued incubation did not alter the results obtained with this antibiotic. Some prophylactic and therapeutic tests were done in mice with strains having 3 different sensitivity patterns: the results of these are somewhat complex, but they suggest, *inter alia,* that spiramycin is more effective than oleandomycin in infection by a strain resistant to erythromycin but sensitive to the other 2 antibiotics. Information is also given about resistance to these antibiotics in *Streptococcus pyogenes* (cross-resistance in this species was complete) and about the sensitivity to them of 2 species of *Clostridium.* *L. P. Garrod*

Buhr, A. J. & Scott, J. C. **Penicillin-Resistant Staphylococci. Incidence in Outpatients with Hand Infections.** *Lancet.* 1959, May 16, 1019–21, 1 fig. [18 refs.]

Of 271 swabs from 267 out-patients with staphylococcal hand infections attending hospital in Oxford in 1957, 81 (30%) yielded penicillin-resistant strains; 5 of 80 resistant strains tested were also resistant to chlortetracycline. 25 swabs were taken from septic lesions in 23 hospital staff; 17 (68%) yielded penicillin-resistant strains. In the general public penicillin-resistant strains were more frequently found if the patient had already had penicillin for the septic lesion; history of earlier penicillin treatment was not available. Records of 58 staphylococci from septic lesions in nurses over the years 1954–8 showed 88% to be penicillin-resistant, with no relation to penicillin treatment. In a comparable study in the same unit in 1952 Scott and Jones (*J. Bone Jt. Surgery,* 1952, v. 34B., 581) found no penicillin-resistant staphylococci in 82 patients examined. *R. E. O. Williams*

Dobrzanski, W. T., Eysymontt, Irena & Osowiecki, H. Charakterystyka szczepów gronkowcowych izolowanych w Klinice Pediatrycznej w Warszawie w latach 1956–1957. [**Characteristics of Strains of Staphylococci isolated in the Pediatric Clinic in Warsaw (1956–1957)**] *Med. Dośw. i Mikrob.* Warsaw. 1958, v. 10, No. 4, 397–408, 1 fig. [20 refs.] English summary.

An investigation has been made of the properties of 287 strains of *Staphylococcus aureus* isolated from 142 patients suffering from staphylococcal infections in a

children's hospital in Warsaw, and also of 27 strains isolated from 10 members of the staff. Of the strains from patients 280 (97·6%) produced coagulase, 276 (96·2%) produced phosphatase and 274 (95·5%) fermented mannitol; only 5 strains were considered to be non-pathogenic. In sensitivity tests with 6 antibiotics 26 strains (9·1%) were sensitive to all antibiotics, 89% were resistant to penicillin and 74 (25·8%) were resistant to penicillin, streptomycin, chloramphenicol, chlortetracycline and oxytetracycline; all except 2 strains were sensitive to erythromycin. Of 272 coagulase-positive strains subjected to phage-typing 79 (29%) were untypable; of the 193 strains which could be typed 103 (53·4%) were of group I, 15 (7·8%) were group II and 50 (25·9%) were group III. 118 strains were susceptible to type 80 phage. All the strains isolated from members of the staff were coagulase-positive and 37% were resistant to penicillin. *D. J. Bauer*

Sasiaw, M. S., Saul, Madelyn, Jenks, Sallie A. & Jablon, J. M. **β-Hemolytic Streptococci from Several Sources Reactive in Both Groups A and F Antisera.** *J. Bacteriology.* 1959, Apr., v. 77, No. 4, 519.

Between 1953 and 1958 some 19,000 throat cultures were examined for the presence of beta-streptococci in the National Children's Cardiac Hospital, in Miami, Florida. About 3,000 cultures of streptococci were recovered and shown to belong to groups A, B, C, F or G, or to be non-typable.

In February 1958, a culture from an excised minced tonsil yielded a beta-haemolytic streptococcus which reacted to both A and F antisera. This characteristic persisted strongly and invariably on repeated subculture of single colonies. Since that time, 3 more persons have been found to harbour organisms reacting with both A and F antisera; all the isolations were from throat cultures and one was recovered from an excised tonsil as well.

3 of the AF cultures have maintained the character of reacting with both A and F antisera through 12 successive generations. *H. J. O'D. Burke-Gaffney*

Pavlov, P. V.; Akimova, V. V.; Pemiankevich, A. N.; Mitel'man, S. L. **Purified Adsorbed Scarlet Fever Toxin—II. Adsorption of Purified Scarlet Fever Toxin** [Pavlov, Akimova & Pemiankevich]. *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, No. 9, 1355–7. **III. Attempts at Active Immunization against Scarlet Fever by means of Purified Adsorbed Scarlet Fever Toxin** [Pavlov, Mitel'man & Akimova]. *Ibid.,* 1358–63. [Translated from Russian.]

II. Aluminium hydroxide was found to be a satisfactory adsorbent for the purified scarlet fever toxin previously described [this *Bulletin,* 1959, v. 34, 574]; borate buffer at *p*H 7·4 was found to be the best solvent. Toxin concentrations corresponding to 1,500–15,000 skin test doses (STD) could be adsorbed by 2·5 mgm. aluminium hydroxide per ml.

III. The aluminium-hydroxide-adsorbed scarlet fever toxin was used to immunize children, in 3 doses of 1,500, 6,000 and 15,000 STD; a booster dose of 6,000 STD was given 5–6 months later. Local reactions occurred in 23% of the children and exanthem in 7·5%; generalized reactions occurred in 2–3%. Reactions were commonest in children who had initially reacted to the least dose of toxin. Revaccination caused no reactions. After immunization only 33% responded to 10 STD and 3·2% to 1 STD. In 15 months after immunization, the incidence of scarlet fever in the 659 inoculated children was 0·9%, compared with 12·5% in the 718 uninoculated [method of selection not stated]. In kindergarten children it was noted that all 4 cases of scarlet fever after inoculation occurred among the 117 initially reacting to 1/3 STD; in 158 similar uninoculated children there were 42 cases.

R. E. O. Williams

Elliott, S. D. & Barnes, Ella M. **Changes in Serological Type and Antibiotic Resistance of Lancefield Group D Streptococci in Chickens receiving Dietary Chlortetracycline.** *J. General Microbiol.* 1959, Apr., v. 20, No. 2, 426–33. [11 refs.]

3 groups of chickens were reared under identical conditions except that one group received 25 p.p.m. chlortetracycline constantly and one group 400 p.p.m. intermittently. Caecal contents were examined for *Streptococcus faecalis* and *Str. faecium* after 12 weeks.

Chlortetracycline-sensitive *Str. faecium* predominated with control birds and the scanty, mainly proteolytic, *Str. faecalis* isolated belonged to 3 serological types D.76, D.15 and H.69D5. Strains of these types have also been isolated from human faeces [this *Bulletin,* 1952, v. 27, 691]. Approximately equal numbers of *Str. faecalis* and *Str. faecium* were isolated from the birds which received small continuous doses of chlortetracycline and *Str. faecalis* dominated in the birds which received larger intermittent doses. All strains of *Str. faecalis* from these groups were chlortetracycline resistant non-proteolytic and type H.69D5.

The effect of withdrawing the antibiotic was tested on the group which received 400 p.p.m. and bulk samples of dejecta tested after 3 and 5 months. 3 months after discontinuing the drug *Str. faecalis* outnumbered *Str. faecium* in control and test groups. Type H.69D5 strains were absent but a chlortetracycline-resistant proteolytic strain of Type D.76 was present in both groups and a sensitive strain of Type D.15 reappeared in the test group. After 5 months the chlortetracycline resistant type D.76 predominated in all birds, the sensitive type D.15 persisted but type H.69D5 was absent.

The authors suggest that the drug-sensitive streptococci originally present were only suppressed, and that on treatment *Str. faecalis* type H.69D5, which rapidly developed resistance, became predominant. The non-proteolytic streptococci of this type may develop resistance more readily than the proteolytic strain.

M. Patricia Jevons

Potter, J. L. & Laskowski, M. **Concerning the Specificity of Streptococcal Deoxyribonuclease (Streptodornase).** *J. Biol. Chem.* 1959, May, v. 234, No. 5, 1263–7, 8 figs. [18 refs.]

RAVIN, A. W. **Reciprocal Capsular Transformations of Pneumococci.** *J. Bacteriology.* 1959, Mar., v. 77, No. 3, 296–309, 1 fig. [21 refs.]

Classical pneumococcal strains A.66 (type III smooth), S.V.III (type III smooth), R.36A (a rough spontaneous mutant of a smooth type II) and strains derived from these were used as recipient strains, and transforming preparations (TP) were prepared from these same strains containing several different transforming factors of which capsular production, streptomycin resistance and erythromycin resistance were used as markers in these experiments. Antibiotic-resistant strains were detected by plating transformed cultures on antibiotic containing plates and capsule production was detected microscopically on blood agar plates and semi-quantitatively by titration with anti-R serum. The preparation of TP and the technique of transformation is described in detail.

Spontaneous S-R mutation rate was fairly low and mutants were phenotypically and genotypically dissimilar as shown by the differences in the ability with which they could be transformed by the various factors in TP and agglutinated by specific antiserum. Many were capable of mutation to the encapsulated condition.

Transforming experiments on R mutants were effected and showed that either there are a large number of independent loci which can mutate to cause suppression of capsular production or a single highly complex one. Transformation to streptomycin resistance could be induced in encapsulated organisms but the frequency decreased as the amount of capsular material synthesized by the host increased. The yield of transformants was highest when there was genetic correspondence between host and donor; contaminating polysaccharide with TP did not appear to be the cause of the diminished yield of transformants.

Reciprocal transformations of strains with normal capsular synthesis to strains of impaired capsular synthesis were effected in experiments in which no spontaneous R mutants were found in control cultures. These cells were agglutinated in low concentrations of anti-R serum only and were isolated in higher numbers among the class of streptomycin resistant transformants than with total treated culture. It was thought that the small fraction of competent bacteria in a transformation mixture make it less likely to find the transformants from the whole culture than from a class that has already been transformed for one character. Some TPs were unable to induce capsule deficient transformants and one recipient strain (A.66) could not be transformed by TP which were competent on other recipient strains.

The response of these reverse transformants to TPs were similar genotypically and phenotypically in respect to capsular character but differed from spontaneous rough mutants of encapsulated strains.

M. Patricia Jevons

PRICE, S. A. & GARE, L. **A Source of Error in Microbiological Assays attributable to a Bacterial Inhibitor in Distilled Water.** [Correspondence.] *Nature.* 1959, Mar. 21, v. 183, 838–40.

The occasional occurrence in well established microbiological assay procedures of irregular and sub-optimal growth leading to discordancy among replicates is well known. The authors have found that folic acid assay with *Streptococcus faecalis R* is particularly prone to this trouble.

The effect varied from one batch of clean assay tubes to another and was traced to a growth inhibitor present in the distilled water used to rinse the tubes in the final stage of the preparation. The effect was not due to chlorine or copper ion.

The inhibitor could be removed by "degassing" the distilled water, that is by boiling it down to 50% of its original volume, by passing the water through a mixed-bed ion exchange column or by treating it with activated charcoal. It could be removed from rinsed tubes by filling them with distilled water and autoclaving them at a pressure of 15 lb./sq.in. for 15 minutes, subsequently draining and drying them before use, or by rinsing them with ethyl methyl ketone (or other, unspecified, solvents).

Infra-red spectroscopy of the ethyl methyl ketone extract suggested that the inhibitor probably consisted of short chain fatty acids. *John R. Norris*

GABRIELESCO, Elena, SUHACIU, G., BORDEIANU, Aurelia, FAUR, Yvonne & ANDREESCO-TIGOIU, Viorica. Modifications histo-pathologiques et histo-chimiques dans le cerveau du cobaye sous l'influence de l'endotoxine B. pertussis. [**Histopathological and Histochemical Alterations in the Brain of the Guineapig under the Influence of *B. pertussis* Endotoxin**] *Arch. Roumaines Path. Expér. et Microbiol.* 1958, Sept.–Dec., v. 17, Nos. 3/4, 483–93, 14 figs. [10 refs.]

The English summary appended to the paper is as follows:—

"1. Inflammatory and degenerative histopathological alterations consisting of oedema and cellular infiltrations in the meninges, nerve tissue and ventricular cavities, and in the formation of perivascular cuffs were noticed to occur in the brain of the guineapig following the intracranial inoculation of B. pertussis endotoxin. Hyperchromatosis, colloidal homogeneization, and vacuolization of cortical and subcortical neurones are described.

"2. The Feulgen reaction discloses a total increase of desoxyribonucleic acid as well as an increase in number and size of Feulgen-positive granules situated on the belt of perinuclear heterochromatin.

"3. The PAS (periodic acid Schiff) reaction in the wall of cerebral vessels decreases during 24 hours following inoculation.

"4. Ventricular lesions were experimentally shown to persist (21 days after toxin inoculation). The clinical significance of the persistence of these lesions after whooping cough is discussed."

EISLER, D. M., KUBIK, G. & PRESTON, H. **Dissociation in *Pasteurella pestis*: [i] Immunological Comparisons of Smooth and Nonsmooth Variants.** *J. Bacteriology.* 1958, Dec., v. 76, No. 6, 589–96, 24 figs. on 2 pls. [23 refs.] [ii] **Interrelations of Smooth and Nonsmooth Variants.** *Ibid.*, 597–606, 4 figs. [24 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin,* 1959, v. 56, 942.]

LARSON, A. D., TREICK, R. W., EDWARDS, C. L. & COX, C. D. **Growth Studies and Plate Counting of Leptospires.** *J. Bacteriology.* 1959, Mar., v. 77, No. 3, 361–6, 3 figs. [19 refs.]

COX and LARSON [this *Bulletin,* 1957, v. 32, 999] described a solid medium on which leptospires would grow and develop colonies visible to the naked eye. The present article records experiments designed to determine whether colony counts on this medium would give a reliable estimate of the number of leptospires present in a culture.

Serial 10-fold dilutions of culture were made and 0·1 ml. aliquots of the dilutions were spread evenly over the surface of duplicate plates. Counts were made when colonies were easily visible, usually after incubation for about 2 weeks. Plates with 20–200 colonies were found to give the most consistent estimates, and were used to calculate the number of leptospires present in the original culture. This figure was compared with that which had been obtained, at the time of inoculating the plates, by a direct count in a Petroff-Hauser counting chamber of a formolized sample of the culture. For the strains of 3 serotypes examined the ratios of total counts to plate count were: *Leptospira biflexa,* 100 : 78; *L. pomona,* 100 : 86; *L. icterohaemorrhagiae,* 100 : 82. It is apparent therefore that the majority of colonies are derived from single leptospires.

To estimate the generation time, plate counts were made of samples taken from cultures during the logarithmic phase of growth. The results are shown in the Table and, commenting on the much longer generation time of *L. icterohaemorrhagiae* grown in Korthof's medium, the authors note that the strains were routinely maintained in Cox's medium and suggest that they may have become in some way more habituated to it.

Certain practical applications of the method of plate culture are suggested. For example, it offers a simple means of purifying cultures contaminated by bacteria, and of ensuring that newly isolated, and also old stock strains consist of a single serotype. It should also prove a useful tool in the study of possible mutation and the production of antigenic variants.

Generation Times of Leptospires

Organism	*Medium*	*Time in hr.*
Leptospira biflexa	Cox	5·8
L. pomona	Cox	9·3
L. icterohaemorrhagiae	Cox	11·6
L. icterohaemorrhagiae	Stuart	10·0
L. icterohaemorrhagiae	Korthof	23·6

J. C. Broom

VAN DER HOEDEN, J. **Leptospiral Infections in Hedgehogs.** *J. Infect. Dis.* 1958, Nov.–Dec., v. 103, No. 3, 225–38. [21 refs.]

Strains of leptospires were isolated from 16 out of 92 hedgehogs caught in different parts of Israel. The 11 strains isolated from 56 *Erinaceus europaeus transcaucasicus* were identified as *Leptospira canicola* (9), *L. ballum* (1) and *L. mini* subtype Szwajizak (1). The 5 strains from 35 *Hemiechinus auritus* were *L. canicola* (4) and *L. grippotyphosa* (1). No evidence of infection was found in the single specimen of *Paraechinus aethiopicus pectoralis* examined.

In absorption tests all 13 Kipod (Hebrew for hedgehog) strains of *L. canicola* completely removed the agglutinins from an antiserum to the type strain (Utrecht IV) of *L. canicola.* By contrast, when an antiserum to *L. canicola* strain Kipod 1 was absorbed with the type strain and with the other 12 Kipod strains, 50–100% of the homologous titre remained.

To explore the possibility that strain Kipod 1 might be a mixture of *L. canicola* and some other serotype, the author carried out a variety of *in vitro* and *in vivo* experiments. [The original should be consulted for details.] All the results indicated that strain Kipod 1 was pure and that it contained an antigenic component in addition to those present in the type strain.

Chronic nephritis, of varying degrees of severity, was noted in some of the infected hedgehogs but no lesions which could be attributed to leptospirosis were present in the others. A 3-month-old *E. europaeus* was infected by instilling culture of *L. mini* into the nostrils and by allowing it to lick culture of *L. canicola* a few days later. The animal sickened and died 9 days after the second exposure. The kidneys showed nephrosis, and numerous leptospires were seen in section of liver and kidney.

Fresh liver and kidney from this hedgehog were fed to a young *H. auritus* which also died of leptospirosis. Leptospires were cultured from the brains of both hedgehogs and proved to be *L. canicola.* No culture of *L. mini* was obtained from the animals.

A strain of *L. canicola* was isolated by inoculating an emulsion of crushed ticks, *Rhipecephalus sanguineus,* into susceptible animals. The hedgehog from which the ticks were collected showed no leptospires in its kidneys and had negative serological reactions. It is presumed therefore that the ticks had acquired the leptospires by feeding on some other animal, and that they may act as natural vectors. [*L. grippotyphosa* was isolated from *Dermacentor marginatus* from cattle by KREPKOGORSKAIA and REMENTSOVA, this *Bulletin,* 1958, v. 33, 180.]

J. C. Broom

CARLQUIST, P. R. **A Simplified Technic for Anaerobic Culture.** *Amer. J. Clin. Path.* 1959, Mar., v. 31, No. 3, 273–5, 1 fig.

The author describes a technique for the anaerobic incubation of single Petri dishes. The lid of the dish is placed rim downwards and the base, containing inoculated medium, is inverted and placed on top of the lid to which it is sealed with hot paraffin wax. Oxygen is removed from the atmosphere within the dish by means of pyrogallic acid and anhydrous sodium carbonate spread over the surface of filter paper on top of the inverted lid. Provided attention is paid to one or two minor points of technique, the oxygen tension is rapidly lowered to a level allowing growth of the most exacting anaerobes.

The use of this technique with blood agar is especially advocated in routine diagnostic work since the colour of the medium indicates the degree of anaerobiosis attained.

John R. Norris

VAN HEYNINGEN, W. E. **The Fixation of Tetanus Toxin by Nervous Tissue.** *J. General Microbiol.* 1959, Apr., v. 20, No. 2, 291–300, 2 figs. [16 refs.]

The author sets himself to reinvestigate, with the improved methods now available, the phenomenon of absorption of tetanus toxin on brain tissue, first observed by WASSERMANN and TAKAKI, which related this absorption to protagon, the component extracted from nervous tissue with hot ethanol after extraction with acetone and ether. In this work a diminution in toxin activity was shown on mixing the toxin with brain tissue and a greater reduction in the toxicity of the supernatant left on removing the nerve tissue by centrifugalization. The test on toxin content of the fluids examined were carried out by injection to mice.

The earlier work was confirmed and protagon and crude phrenosine were found to be at least equal to whole beef brain (dry weight) when the extraction was done with small doses of toxin, of the order of 10 LD50. When, however, the same substances were investigated with much larger doses of toxin, as *e.g.* 20 L +, the tetanus-fixing capacity of protagon was found greatly to exceed that of whole beef brain or grey matter. No convincing explanation of this anomaly is brought forward.

All attempts to separate an active substance from protagon were unsuccessful up to this stage.

J. W. McLeod

VAN HEYNINGEN, W. E. **Chemical Assay of the Tetanus Toxin Receptor in Nervous Tissue.** *J. General Microbiol.* 1959, Apr., v. 20, No. 2, 301–9, 5 figs. [13 refs.]

In pursuit of the investigation described above, the author sought a simpler, quicker and less expensive method than the biological one for testing out the toxin combining power of a large range of substances and preparations obtained from nervous tissue. For these observations a toxin obtained from the Wellcome Research Laboratories was used which contained 40·8% of protein and carried 360 L + doses/mgm. of protein, *i.e.* its purity was 75% of that described for the more highly purified crystalline preparations. Protein content was determined by a colour reaction, that of Folin-Ciocalteau. It was demonstrated that, where the toxin was absorbed from a crude preparation by a suspension of protagon from which the absorbed protein was then extracted with 0·1 N sodium hydrate, a solution was obtained which gave the ultraviolet absorption of pure protein. Further, when a series of absorptions were made with graded amounts of protagon and the absorbed toxin was estimated by the biological method, the correlation between L + doses of toxin and the amount of protein, estimated chemically, showed a very close correspondence. Further tests were made of the absorption by protagon of tetanus toxins, tetanus toxoid, dysentery toxin, diphtheria toxin, *Clostridium welchii* toxins, and crystalline preparations of trypsin, pepsin and lysozyme, as well as of purified serum albumin and α and β globulins. There was slight absorption of all the substances but rather more of lysozyme and of tetanus toxoid. The absorption of toxin, however, was very much greater than that of any of the other substances and this was shown to be still more so if the ionic salt content of the fluid in which the protagon was suspended was 0·15 or more. A concentration of 60 L + of toxin was selected as that likely to give the best results.

J. W. McLeod

VAN HEYNINGEN, W. E. **Tentative Identification of the Tetanus Toxin Receptor in Nervous Tissue.** *J. General Microbiol.* 1959, Apr., v. 20, No. 2, 310–20, 3 figs. [17 refs.]

Using the chemical method already described above for determining the toxin absorbing capacities of various components of the nervous tissue, the author has come to the conclusion that the complex actually responsible for the absorption shown by protagon is a ganglioside. The ganglioside is water-soluble but apparently exists in the form of insoluble complexes with water-insoluble cerebrosides and sphingomyelins. It is suggested that a contaminant of the ganglioside, such as strandin, may be actually responsible for the fixation of the toxin but, in view of the lack of exact information about the composition of gangliosides, it is not possible to carry the matter further at the present moment.

J. W. McLeod

BONI, A. Sensibilità agli antibiotici delle spore batteriche *in vitro*. Nota III. Sensibilità delle spore di *C. tetani* in varie condizioni sperimentali. [**Sensitivity of Bacterial Spores to Antibiotics *in vitro*. III. Sensitivity of *Clostridium tetani* Spores in Different Experimental Conditions**] *Riv. Istituto Sieroterap. Ital.* 1959, Jan.–Feb., v. 34, No. 1, 12–21. [18 refs.] English summary (5 lines).

The range of antibiotics tested was the following: potassium salt penicillin G; dihydrostreptomycin base; polymyxin B; bacitracin; the tetracyclines; oleandomycin base; oleandomycin-tetracycline mixture; chloramphenicol.

4 strains of tetanus were tested. For 3 of these penicillin was inhibitory of growth in lower concentration than any of the other substances. It was, however, considerably weaker against the Harward strain than the tetracyclines. The combination of oleandomycin and tetracycline appears to restrain growth to a greater extent than could be explained by the summation of the actions of the 2 separate substances. No satisfactory evidence of the killing of spores was obtained.

The general recommendation is made that, in view of the activity of the tetracyclines against all the strains tested, these, or the oleandomycin-tetracycline mixture, either of which could be administered by mouth, should form part of the standard prophylactic treatment of wounds with a view to the elimination of tetanus.

J. W. McLeod

MURATA, R., YAMADA, T. & KAMEYAMA, S. **Production of Alpha Toxin of *Clostridium perfringens*. I. Preparation of the Reproducible Peptone Medium for the Production of the Toxin of High Potency.** *Japanese J. Med. Sci. & Biol.* 1956, June, v. 9, No. 3, 81–91, 2 figs. [11 refs.]

"1. A peptone medium is described on which *Clostridium perfringens PB6K* is able to yield a potent alpha toxin of 200–300 E.U., *i.e.* approximately 600–900 LD_{50}, and some factors affecting the toxin production were discussed.

"2. Some divalent metallic ions such as Zn++ and Mn++ are beneficial in combination with vitamin mixture.

"3. Fructose can successfully be substituted for dextrin on the peptone medium."

PENSO, G. & VICARI, G. Studio dei fenomeni immunitari per mezzo delle colture di tessuto. IV. Sull' azione citopatogena della tossina di *Clostridium histolyticum*. [**The Study of Immunity Phenomena by means of Tissue Cultures. IV. The Cytopathogenic Action of the Toxin of** *Clostridium histolyticum*] *Rendiconti Istituto Superiore di Sanità*. Rome. 1959, v. 22, Pt. 2, 131–4, 2 coloured figs. on pl. V. Sull'azione citopatogena della tossina di *Clostridium septicum*. [**V. The Cytopathogenic Action of the Toxin of** *Clostridium septicum*] *Ibid.*, 135–7, 2 coloured figs. on pl. VI. Sull'azione citopatogena della tossina di *Clostridium oedematiens*. [**VI. The Cytopathogenic Action of the Toxin of** *Clostridium oedematiens*] *Ibid.*, 138–40, 3 coloured figs. on pl.

The English summaries appended to the paper are as follows:—

IV.—"The toxin of *Clostridium histolyticum* has a cytopathogenic action on all the types of tissue cultures we have tested: human liver (Chang strain); human kidney; monkey kidney; buccal carcinoma (K.B. strain).

"Such an action becomes evident after a period of incubation of two or more hours, with a vacuolar degeneration of the protoplasm, not due to processes of steatosis, which is followed by a cellular retraction and nuclear pycnosis, and ends with the death and partial detachment of the cells."

V.—"The toxin of *Clostridium septicum* has cytopathogenic action on all types of tissue cultures which we have tested: human liver (Chang strain); human kidney; monkey kidney; buccal carcinoma (K.B. strain).

"Such an action becomes evident after a period of incubation of about 1 hour, with hyperchromia of the nuclei followed by a degeneration of the cellular cytoplasm, which loses its homogeneous aspect, becomes undelimited and rapidly disintegrates: the cells die and detach completely after 6 hours."

VI.—"The toxin of *Clostridium oedematiens* has cytopathogenic action on all types of tissue cultures which we have tested: human liver (Chang strain); human kidney; monkey kidney; buccal carcinoma (K.B. strain).

"Such an action becomes evident after 4 hrs of incubation with pycnosis of the nucleus and contraction of cytoplasm; these degeneration processes evolve and complete in about 24 hrs. The cytoplasm of the cells assume the shape of a ring surrounding a hyperchromic nucleus; the cells die without getting detached from the wall of the culture tube."

REYMOND, A., BOZIC, C. & GRANDUILLAUME, P. La listériose. A propos de deux observations de listériose foetale et néonatale. [**Two Cases of Foetal and Neonatal Listeriosis**] *Schweiz. med. Woch.* 1959, May 9, v. 89, No. 19, 495–9, 5 figs. [17 refs.]

The English summary appended to the paper is as follows:—

"Anatomo-clinical report of two autochthonous cases of fetal and neo-natal listeriosis, one by hematogenous transplacental infection, the other by amniotic ascending infection. The pathogenesis of congenital listeriosis is briefly discussed."

[See also this *Bulletin*, 1958, v. 33, 1087.]

FUNGI

ECKSTEIN, Z., HALWEG, Halina, KRAKÓWKA, Paweł & URBANSKI, T. O działaniu fungistatycznym kwasu, 3,4 - dwuchlorofenoksyacetohydroksamowego na grzyby chorobotwórcze *in vitro*. [**The Fungistatic Activity of 3,4-Dichlorophenoxyacetohydroxamic Acid on Pathological Fungi** *in vitro*] *Med. Dośw. i Mikrob.* Warsaw. 1958, v. 10, No. 4, 487–92, 2 figs. English summary (8 lines).

8 aryloxyacetohydroxamic acids have been examined by the cylinder plate method for the presence of fungistatic activity against a number of pathogenic fungi. The most effective compound was 3 : 4-dichlorophenoxyacetohydroxamic acid, which inhibited the growth of *Candida albicans, Cryptococcus neoformans* and 4 species of *Trichophyton*. The range of activity of the compound was examined further in tests with 18 pathogenic fungi, in which the minimum inhibitory concentrations were determined in tube tests in liquid Sabouraud medium. In all cases inhibition of growth was obtained with concentrations ranging from 0·004 to 0·5 mgm. per cc., the highest activity being seen with *Histoplasma capsulatum*. *D. J. Bauer*

BLASCHKE-HELLMESSEN, Renate. Ungewöhnliche morphologische Veränderungen bei pathogenen Hautpilzen durch antimykotisch wirkende aerobe Sporenbildner. [**Unusual Morphological Changes in Dermato-Pathogenic Fungi produced by Aerobic Spore-Forming Bacilli with Antimycotic Activity**] *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 175, Nos. 3/4, 282–305, 19 figs. [13 refs.]

CATANEI, A. & SCHOUSBÖE, A. Étude morphologique et expérimentale de deux souches algériennes d'*Achorion schönleini* ayant provoqué du favus généralisé et mortel. [**Morphological and Experimental Study of 2 Algerian strains of** *Achorion schönleini* **responsible for Generalized and Fatal Favus**] *Arch. Inst. Pasteur d'Algérie*. 1958, June, v. 36, No. 2, 153–8.

This is a cultural study, over an extended period, of two strains of *Achorion schönleini* isolated from lesions

of the scalp and glabrous skin of two Musulman children aged 10 years and 9 years who succumbed to a generalized infection caused by this organism. The cultural features observed in a succession of subcultures, mainly on Sabouraud medium containing glucose, showed that, whereas cultures obtained from the scalp varied in character within the range known for *A. schönleini*, cultures obtained on this medium from other sites showed variations which, in the authors' opinion, were not characteristic of the species. The most notable of these was a pigmentation which was yellow, apricot or ferruginous. Another variation was the late development (after a number of subcultures) of the cerebriform configuration usually associated with cultures of this species, or in some isolates, its virtual disappearance after repeated subculture. Pathogenicity of these strains for guineapigs was apparently not enhanced as a result of their being the cause of a generalized and fatal type of the disease.

C. J. La Touche

LEVINE, S., EVANS, E. E. & KABLER, P. W. **Studies of *Cryptococcus* Polysaccharides by Infrared Spectrophotometry.** *J. Infect. Dis.* 1959, May–June, v. 104, No. 3, 269–73, 1 fig.

GORDON, Ruth E. & MIHM, Joan M. **A Comparison of *Nocardia asteroides* and *Nocardia brasiliensis*.** *J. General Microbiol.* 1959, Feb., v. 20, No. 1, 129–35. [13 refs.]

The morphological characteristics (both macroscopic and microscopic) and the physiological characteristics of a number of old and recently isolated strains of *N. asteroides* and *N. brasiliensis* are compared, and also the chief characteristics in which they differ from other species are indicated. It is pointed out that characters such as acid-fastness which are reliable in the diagnostic laboratory in freshly isolated strains of these 2 species may not be revealed by older strains. The authors are satisfied that their analyses of these strains fully substantiate the claims of other authors for the recognition of *N. asteroides* and *N. brasiliensis* as 2 distinct species.

C. J. La Touche

CASTELLANI, A., DE BRITO, Maria M. X. & PINTO, M. R. **An Actinomycete isolated from an Autochthonous Case of Mycetoma in Portugal.** *J. Trop. Med. & Hyg.* 1959, Feb., v. 62, No. 2, 27–36, 9 figs. (1 coloured).

In this paper the authors describe in detail the morphological and physiological features (in culture) of an actinomycete-like organism isolated from a yellow-grain-type mycetoma. Its chief distinguishing characteristics appear to be the following:—on 2% glucose agar and on Czapek agar growth is "abundant, nodular or irregularly heaped up", and is coloured red or purplish; on maintenance agar it is less abundant and is lacking in pigmentation; macroscopic aerial mycelium is not produced and no earthy or musty smell can be detected; the mycelium, as studied by light and electron microscopy, is composed of slender, branching hyphae 0·5–1·2 microns, or occasionally more, in thickness; fasciculation of the hyphae, "Kleinberger-Nobel" nests and bridge-hyphae may also be observed; of particular interest is a method of reproduction which it possesses in addition to fragmentation of the mycelium: this is by means of globose to fusiform "conidia" borne singly at the tips of the hyphae. For this organism the authors tentatively claim new generic and specific rank by proposing for it the binomial *Actinomonospora lusitanica* Castellani, de Brito, Pinto.

C. J. La Touche

SEGRETAIN, G. & MARIAT, F., with the technical collaboration of J. SATRE. Contribution à l'étude de la mycologie et de la bactériologie des mycétomes du Tchad et de la Côte des Somalis. [**Mycological and Bacteriological Studies of Mycetomas in Tchad and in the Somali Coast**] *Bull. Soc. Path. Exot.* 1958, Sept.–Oct., v. 51, No. 5, 833–62, 1 text fig. & 16 figs. on 4 pls. [29 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 980.]

BACTERIOPHAGES

TERADA, Masanaka. **Studies on Bacterial Viruses.** 153 pp., 81 figs. 1956. Tokyo: Naya Publishing Co., Ltd.

This is not a textbook but a report summarizing work done on phages in the author's laboratory during the 10 years up to 1956. It should be said at the beginning that no outstandingly original contribution has been made. There is no theme to the book and no index. On the other hand, a lot of work, mostly of a descriptive kind, has been done on the properties of some phages not among those popularly studied.

The first few chapters contain electron micrographs and brief descriptions of 25 virulent phages isolated from organisms ranging from *Salmonella* to bacteria parasitic on plants and to *Actinomyces*. The resistance of these phages to heat, *p*H, some chemicals and to some antibiotics, is summarized. Resistant mutants of various kinds were selected and it was shown that they retained their resistance on passage in media free from the agents concerned. A search was made for the presence of enzymes in purified phage preparations. Enzymes concerned in carbohydrate metabolism and in the Krebs tricarboxylic acid cycle were not found. Catalase activity was found, however, in a *Salmonella* phage, even when it had been grown in a host free from catalase. During the purification process the enzyme was found to accompany the phage at each stage, and not the contaminating protein. There is a chapter on the serological relations of 10 *Salmonella* phages, and of some actinophages. No serological relationship was found between the phage and the host it was grown on. The report ends with an account of some genetic experiments done on recombination between *Salmonella* phages, on the mutation to heat

resistance, on the conversion to I antigen, and on the inheritance of the ability to produce sectored plaques.

The contents of the book have been set out here in some detail because it is not a book that the general reader would ordinarily wish to buy, though specialists may find something of interest in it.

Janice Taverne

UETAKE, H. **The Genetic Control of Inducibility in Lysogenic Bacteria.** *Virology.* New York. 1959, Mar., v. 7, No. 3, 253–62, 2 figs. [19 refs.]

Antigen 10 of *Salmonella anatum* 293 E_1 is converted by lysogenization with phage ϵ^{15} to antigen 15. The lysogenic strain carrying ϵ^{15} can be induced by UV light, but 2 derivatives isolated from it failed to be induced. The first derivative was a defective lysogenic strain, which possessed antigen 15 but was as sensitive to UV as the original unlysogenized strain. Its inability to be induced by UV was shown to have resulted from a change in the host cell by the following experiment: The defective cells were cultured in broth containing antiserum to antigen 15 and a strain was obtained which carried antigen 10 and adsorbed phage ϵ^{15}, presumably because it had lost the defective prophage. When this strain was relysogenized with ϵ^{15}, it could not be induced by UV light. Phage isolated from it and made to lysogenize the original strain was inducible in the normal way. Thus, the loss of inducibility was due to a genetic change in the bacterial cell, which persisted after the prophage was lost. This property was shown to be specific for phage ϵ^{15} and was not transferable to other cells by the phage.

The second non-inducible strain was lysogenic for a mutant phage ϵ^{15}b. The phage itself was inducible, suggesting that, as before, a change had occurred in the host cell.

It is generally accepted that inducibility is a hereditary prophage character. These 2 examples indicate that it is under the dual control of phage and of bacterial genes. In both cases the phage itself had also undergone mutation, in the first instance to defectiveness, in the second to ϵ^{15}b. It is suggested that the mutational event removed the prophage to a "noninducible" region of the chromosome, and that in this process, which was probably in the nature of recombination, the prophage itself was genetically altered.

It is also pointed out that when a phage is defective and cannot be induced, the phage control of antigens will not be recognized. *Janice Taverne*

SIX, E. **The Rate of Spontaneous Lysis of Lysogenic Bacteria.** *Virology.* New York. 1959, Mar., v. 7, No. 3, 328–46, 2 figs.

The rate of spontaneous lysis of lysogenic bacteria has been measured on agar plates by a method which does not require knowledge of the burst size. Lysogenic cells, mixed with anti-phage serum to kill free phage, were diluted and plated with streptomycin-resistant *Shigella dysenteriae.* At intervals, the plates were sprayed with streptomycin to kill the lysogenic cells. Any plaques formed on the streptomycin-resistant indicator therefore arose from cells which had lysed before streptomycin was added. The number of colonies formed by the lysogenic cells was also determined.

Several lysogenic strains of *Escherichia coli* C and of *Sh. dysenteriae* Sh carrying 1, 2 or 3 prophages of P2 and its variants were studied. It was found that, for any given strain, the results were consistent with the idea of a constant rate of spontaneous lysis with unit time, independent of the generation time. The rate of spontaneous lysis did not vary with the genetic markers of the prophage employed, nor was it affected by the presence of an unrelated prophage. It did, however, vary with the genetic state of the host; different rates of lysis were obtained with *E. coli* C and *Sh. dysenteriae* Sh carrying the same prophage, and with *E. coli* C carrying the prophage at different locations. The rate of spontaneous lysis was not proportional to the number of P2 prophages per nucleus.

Janice Taverne

LIPNICKI, B. & WOJCIECHOWSKI, Z. Działanie związków biguanidynowych na bakteriofaga czerwonkowego. **[The Action of Biguanidine Compounds on Dysentery Phage]** *Archiwum Immunol. i Terapii Dośw.* Warsaw. 1959, v. 7, No. 1, 163–70, 1 fig. [19 refs.]

"1. Using the described technique the action of 29 derivatives of biguanidine, amidourea, amidothiourea and cyclic derivatives on free particles of dysenteric phage, its intracellular multiplication and adsorption to the detector cells were examined.

"2. The preparations: T 222 (N_1-p-chlorphenyl-N_2-amidineurea hydrochloride) and T 259 (N_1-p-bromphenyl-N_2-amidineurea) at the concentration of 1000 μg/ml exert, after 24 hour incubation, a destructive effect on free particles of *Shigella flexneri* dysentery phage.

"3. T 222 and T 259 preparations have no effect on adsorption and intracellular multiplication of this phage."

KANTOCH, M. Badania nad fagocytozą wirusów bakteryjnych. Doniesienie I. **[Studies on the Phagocytosis of Bacterial Viruses. I]** *Archiwum Immunol. i Terapii Dośw.* Warsaw. 1958, v. 6, No. 1, 63–84. [17 refs.] English summary.

Guineapigs were inoculated intraperitoneally with sterile broth in order to produce a leucocytic effusion and were then injected with T2 phage by the same route; in samples of exudate withdrawn after 5 hours and plated on the indicator organism a considerable amount of phage was found attached to the leucocytes. Attempts to liberate the phage by lysing the leucocytes with 0·1% sodium hydroxide solution caused some loss of titre. Some phage was still found to be associated with the leucocytes after treatment with phage antiserum, and it is concluded that phagocytosis of phage had taken place to a certain extent.

D. J. Bauer

BRENNER, S. & SMITH, J. D. **Induction of Mutations in the Deoxyribonucleic Acid of Phage T2 Synthesized in the Presence of Chloramphenicol.** [Correspondence.] *Virology*. New York. 1959, May, v. 8, No. 1, 124–5.

LITMAN, Rose M. & PARDEE, A. B. **Mutations of Bacteriophage T2 Induced by Bromouracil in the Presence of Chloramphenicol.** [Correspondence.] *Virology*. New York. 1959, May, v. 8, No. 1, 125–7, 1 fig. [10 refs.]

HELPRIN, J. J. & HIATT, C. W. **Photosensitization of T2 Coliphage with Toluidine Blue.** *J. Bacteriology*. 1959, Apr., v. 77, No. 4, 502–5, 3 figs. [15 refs.]

"A study of the inactivation of T2r+ and T3 coliphages by the photodynamic action of toluidine blue has demonstrated that these phages differ widely in rate of uptake and tenacity of binding of the photosensitizing dye. The reaction of the dye with T2 phage is very slow, has a high temperature coefficient (Q_{10} = 3.8), and illustrates the selective permeability of the T2 phage membrane. The rate of photodynamic inactivation of T2 phage depends greatly upon the state of completion of this dye-virus reaction. The uptake of dye by T3 phage, on the other hand, is very rapid and is readily reversible."

[See also this *Bulletin*, 1958, v. 33, 798.]

KRIEG, D. R. **A Study of Gene Action in Ultraviolet-Irradiated Bacteriophage T4.** *Virology*. New York. 1959, May, v. 8, No. 1, 80–98, 2 figs. [22 refs.]

"The action of individual *r*II+ genes of bacteriophage T4 was analyzed by crosses between ultraviolet-sterilized wild-type phage and unirradiated phage mutant for the gene being investigated. Inactivation of a gene (i.e., loss of its capacity for phenotypic action) was characterized by a single-hit relation to dose, with a sensitivity of 0.10 and 0.05 per phage-lethal damage for the A and B cistrons, respectively. The presence of an *r*II+ gene in the progeny of a cross was also studied. This phenomenon, called cross reactivation (CR), involves genetic duplication and recombination of irradiated phage. In some experiments doubly mutant phage was used for simultaneous analyses of two genes. The interpretation of these experiments is based on the assumption that cistrons (genes, or, more precisely, genetic units of fuction) occupy certain lengths along the phage linkage structure ("chromosome"). A radiation-induced damage on this chromosome will inactivate a phage, but a phage's undamaged components may act in a mixed infection. A damage located anywhere within a cistron destroys its capacity for phenotypic action. Undamaged specific genetic elements may be rescued by CR. "Survival of phenotype" (SP) is not normally a prerequisite for CR; in these experiments, however, survival of the phenotype of the particular *r*II+ gene being investigated was a necessary (but not sufficient) condition for CR.

"The experiments are discussed with regard to the role of phage genes in initiating infection and with regard to radiation genetics, with particular attention to cross reactivation and multiplicity reactivation of bacteriophage."

PIETRZYKOWSKA, I. **The Role of Protein Synthesis in the Production of the Lysogenic Phage after UV Induction.** *Bull. Acad. Polonaise des Sci.* Warsaw. Sér. Sci. Biol. 1959, v. 7, No. 5, 177–82, 3 figs. [15 refs.]

When chloramphenicol was added to lysogenic *Escherichia coli* K 12 at intervals after induction with UV light, the production of phage λ was found to be inhibited. The longer the period for which chloramphenicol was present, the longer the latent period before lysis after its removal. The increase in the length of the latent period, as well as the reduction in burst size, was related to the time after induction when chloramphenicol was added. The drug caused most effect when added immediately after induction.

Thus, as with virulent phages, (*e.g.* TOMIZAWA and SUNAKAWA, *J. General Physiol.*, 1956, v. 39, 553) protein synthesis is shown to be necessary for the production of a temperate phage. Protein synthesis appears to be concerned, also, in the change from prophage to vegetative phage which follows immediately upon induction. The effect of chloramphenicol added immediately after induction could not be reversed by removing it during the first 20 minutes, although it is known that changes occurring during this interval can be reversed by photoreactivation. *Janice Taverne*

VIRUSES

In this section the abstracts are arranged as far as possible in the following order: General Psittacosis-lymphogranuloma viruses; Pox Viruses; Respiratory and other viruses; Enteric viruses; Arthropod-borne viruses; others.

FENNER, F., HOLMES, I. H., JOKLIK, W. K. & WOODROOFE, Gwendolyn M. **Reactivation of Heat-Inactivated Poxviruses: a General Phenomenon which includes the Fibroma-Myxoma Virus Transformation of Berry and Dedrick.** [Correspondence.] *Nature*. 1959, May 9, v. 183, 1340–41.

Using strains of vaccinia virus with well-differentiated biological characters, the authors found that if mixtures of heat-inactivated virus of one strain and infectious virus of another strain were inoculated into mouse brains, they recovered infectious virus of the inactivated strain as well as of the active strain and recombinant strains. This reactivation phenomenon was demonstrated in cultures of HeLa cells and in chick embryo chorio-allantois. Reactivation occurred when the active virus was cowpox, ectromelia, myxoma, fibroma or fowlpox. There was no reactivation when the active

component came from groups other than poxviruses. Treatment of the inactivated virus by trypsin or deoxyribonuclease or heating at 55°C. for as long as 7 hours does not destroy the capacity for reactivation.

Colin Kaplan

SPIES, K. & EDLINGER, E., with the technical assistance of M. SCHOEDE & C. KORB. Vermehrung und Weiterzüchtung eines dermotropen bovinen Vaccine-Stammes in mesodermalen Zellen (L-Stamm, Earle) *in vitro*. **[Multiplication and Passage of a Dermotropic Bovine Vaccinia Virus Strain on Mesodermal Cell Cultures (L-Strain, Earle)]** *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 174, Nos. 1/2, 29–37, 3 figs. [25 refs.]

A commercial dermotropic vaccine strain of vaccinia virus was adapted to chick embryo chorio-allantois and then used to infect monolayer cultures of Earle's L-strain mouse cells. The authors found that infected cells were agglutinated. Cell destruction then occurred in the centre of the agglutinated mass. Virus multiplication was demonstrated in these cultures. This is contrary to the finding of RYDEN and RANDALL [this *Bulletin*, 1957, v. 32, 812] that only a mouse neurotropic strain of vaccinia virus would multiply in L-strain cells. The authors suggest that this was because the dermatropic strain of virus used by the previous workers had been passaged for a very long time in chick embryo chorio-allantois. [In view of the relative ease with which vaccinia virus can be grown in new hosts and different tissues, this explanation is probably inadequate.] *Colin Kaplan*

PUMPER, R. W. **Differences in Response of Tissue Culture Cell Lines to Vaccinia Virus.** *Amer. J. Hyg.* 1959, Mar., v. 69, No. 2, 79–82, 4 figs.

The cell lines used in this work were mouse lung, guineapig lung, and Earle's strain L mouse fibroblasts. Vaccinia virus infection of L cells led to plaque formation in 3 or 4 days and complete destruction of infected cells in 4 to 6 days. With both mouse and guineapig lung cells, however, the initial change seen was a swelling of cells at about 20 hours after infection. At about 60 hours the swollen cells had largely disappeared, giving place to plaques with abnormal cells at the periphery. *Colin Kaplan*

CASSEL, W. A. & FATER, Barbara. **Loss of Hemagglutinin on Passage of Vaccinia Virus in L Cells.** *Proc. Soc. Exper. Biol. & Med.* 1959, Mar., v. 100, No. 3, 629–30.

Vaccinia virus passaged in Ehrlich tumour cells of mice loses its ability to produce haemagglutinin. Cell-free peritoneal fluids from mice carrying Ehrlich carcinoma contain an inhibitor of vaccinia haemagglutinin. When virus was passaged in cultures of L cells in medium without Ehrlich inhibitor, haemagglutinin continued to be formed. Passage in the presence of inhibitor led, after a number of passes, to loss of ability to produce haemagglutinin. Subsequent repeated passage in chick embryos was followed by recovery of haemagglutinin-forming ability: the longer the passage series in inhibitor, the longer it took to recover haemagglutinin. After 24 or more passages in inhibitor in L cell cultures, the haemagglutinin was not recovered in 31 passages in chick embryos.

Colin Kaplan

MCREA, J. F. & O'LOUGHLIN, Jean. **Separation of Vaccinia Haemagglutinin from Infectious Virus Particles by Chromotography on DEAE Columns.** [Correspondence.] *Virology*. New York. 1959, May, v. 8, No. 1, 127–9, 1 fig.

MAGEE, W. E. & SAGIK, B. P. **The Synthesis of Deoxyribonucleic Acid by HeLa Cells Infected with Vaccinia Virus.** [Correspondence.] *Virology*. New York. May, v. 8, No. 1, 134–7. [12 refs.]

WELLER, T. H., WITTON, Helen M. & BELL, E. J. **The Etiologic Agents of Varicella and Herpes Zoster. Isolation, Propagation, and Cultural Characteristics** *in Vitro*. *J. Exper. Med.* 1958, Dec. 1, v. 108, No. 6, 843–68, 1 text fig. & 33 figs. on 7 pls. [30 refs.]

14 strains of varicella and 8 strains of zoster virus have been isolated from vesicle fluids and maintained in cultures of human embryo skin muscle or preputial tissue; varicella was maintained through 38 passages over a total period of 799 days, and zoster through 28 passages over 678 days. Passage was carried out with infected cells, and cytopathic changes could be observed after 2 days and involved 50% of the cell sheet after 15–30 days. They took the form of foci of rounded refractile cells with varying numbers of giant cells, and spread by direct involvement of adjacent cells. Multiplication of the viruses could also be supported by HeLa and other cells of human origin, and by cultures of a number of a monkey tissues. [The paper contains a great deal of detailed information and should be studied in the original by those who wish to work with these viruses.] *D. J. Bauer*

WELLER, T. H. & WITTON, Helen M. **The Etiologic Agents of Varicella and Herpes Zoster. Serologic Studies with the Viruses as propagated** *in Vitro*. *J. Exper. Med.* 1958, Dec. 1, v. 108, No. 6, 869–90, 2 text figs. & 2 figs. on pl. [21 refs.]

In attempts to prepare complement-fixing antigens from human embryo skin-muscle tissue cultures infected with varicella and zoster viruses it was found that the antigenic potency of the culture fluid was insufficiently high, but satisfactory antigens could be obtained by concentrating the fluid about 25-fold by ultrafiltration by the method of SEIBERT as modified by SVEDMYR [this *Bulletin*, 1952, v. 27, 897]. The antigens were slightly anticomplementary after heating at 60°C. for 30 minutes, but a repetition of the heating reduced the effect to a satisfactory level. In complement-fixation tests carried out on 137 sera from 52 patients with varicella and 53 sera from 29 patients with zoster it was found that antibody appeared 4–5 days after the appearance

of the exanthem in varicella and continued to rise during the second week of illness; a similar course was observed in zoster, although significant titres of antibody were sometimes present at the beginning of illness, and a rise of titre did not always occur. Satisfactory antigens could also be prepared from monkey kidney cultures, and from extracts of infected human skin-muscle tissue obtained by freezing, thawing and centrifugation. Incomplete neutralization of the cytopathic effect could be observed when the immune sera were added to the culture medium. The results of the complement-fixation and neutralization tests confirmed the close antigenic relationship thought to exist between the 2 viruses. *D. J. Bauer*

Schwartz, J., Elias, H., Moscovici, O. & Samuel, I. Izolarea virusului urlian din lichidul cefalorahidian. Studiul tulpinilor. [**Isolation of Mumps Virus from the Cerebrospinal Fluid. A Study of the Strains**] *Studii si Cercetări Inframicrobiol., Microbiol. si Parazitol.* 1958, v. 9, No. 1, 51–4. [10 refs.] French summary.

4 strains of mumps virus have been isolated by means of amniotic infection of 7-day-old chick embryos with cerebrospinal fluid from 3 children who were suffering from mumps meningoencephalitis, and from another child in whom a cellular reaction had been found on lumber puncture in the absence of clinical involvement of the central nervous system. One strain could be carried through 37 amniotic and 29 allantoic passages. The strains showed slight differences in their infectivity and haemagglutinin titres. 2 strains produced keratitis in guineapigs after inoculation into the anterior chamber. *D. J. Bauer*

Smorodintsev, A. A. & Klyatchko, N. S. **Live Anti-Mumps Vaccine. I. Results of Tests of the Immunogenic Properties of Live Vaccine when administered intradermally to Susceptible Children.** *Acta Virologica.* Prague. 1958, July–Sept., v. 2, No. 3, 137–44, 4 figs. [20 refs.]

Mumps vaccine containing live virus was prepared from pooled infected amniotic fluids by dialysis for 20 hours at 4°C. against tap-water or saline; it was stored at 0–4°C. for 1 month or preserved by freeze-drying. 10 adult volunteers were treated with the vaccine by application to the oral mucosa in the region of the orifice of the parotid duct; no reactions occurred and no formation of antibody could be detected. 90 adult volunteers were given an intradermal injection of 0·1 ml. of vaccine, and inhibiting and complement-fixing antibodies appeared in 40% and 70% respectively. The vaccine was tested further by intradermal inoculation in 150 children aged 4–14 years. Erythema 5–30 mm. in diameter developed at the site of inoculation within 24 hours and disappeared within 2–3 days. A rise in inhibiting antibody was observed in 75% of children, but the titre declined after 3 months. The percentage of positive reactions to mumps skin test antigen also increased after vaccination, and remained at a high level for 18 months. *D. J. Bauer*

Klyatchko, N. S. & Smorodintsev, A. A. **Live Anti-Mumps Vaccine. II. Epidemiological Effectiveness of the Immunization of Children with a Single Intradermal Injection of Live Anti-Mumps Vaccine.** *Acta Virologica.* Prague. 1958, July–Sept., v. 2, No. 3, 145–51, 2 figs.

In 1955–6, 4,116 children aged 3–6 years attending 157 kindergartens in Leningrad were given a single intradermal injection of the live mumps vaccine described in the preceding paper, and the subsequent incidence of mumps was recorded over a period of 1½ years in comparison with a control group of 5,567 unimmunized children attending the same kindergartens. Mumps occurred in 103 kindergartens during the period of observation; there were 423 cases among the control group (7·58%) and 30 among the vaccinated children (0·73%), the coefficient of effectiveness of vaccination thus being 10·4. In other kindergartens in which vaccination had not been carried out 70 cases of mumps occurred among 614 children (11·4%). The immunity produced by vaccination persisted for at least 18 months. The few cases of mumps which occurred in vaccinated children were mild and did not give rise to extensive outbreaks. *D. J. Bauer*

Kliachko, N. S., Kuz'min, P. I. & Mikhailov, I. M. **Results of the Study of the Infectious, Reaction-Producing and Antigenic Effects of Dried Preparations of Live Attenuated Mumps Vaccine.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1957, v. 28, Nos. 7/8, 989–94. [Translated from Russian.]

In an attempt to reduce the cost of live mumps vaccine prepared from infected amniotic fluid an investigation has been made of the immunological effectiveness of a vaccine consisting of pooled amniotic and allantoic fluids. The infectivity titres of 4 batches of vaccine of this type were around 7 log units, and were not greatly below the titres of amniotic vaccines, which were usually around 7–8 log units. In lyophilization tests it was found that the loss of titre due to drying could be reduced to 0·5–0·7 log unit by adding 10% of gelatin or 10% of sucrose with 10% of yolk as stabilizers. In tests carried out on 26 children aged 3–7 years who had not previously suffered from mumps the intradermal injection of 0·1 cc. of redissolved dried vaccine produced a marked skin reaction which disappeared after 2–3 days; a general reaction was observed in only 1 instance. A rise in inhibiting antibody titre of 4 times or greater appeared in 19 children (73·1%). *D. J. Bauer*

Bronitki, A., Petrescu, A., Petrescu, P., Rothschild, L. & Athanasiu-Stroescu, P. Izolarea unei tulpini gripale cu caracter predominant neurotrop, dintr-un caz letal la sugar. [**The Isolation of a Strain of Influenza Virus of Predominantly Neurotropic Character from a Fatal**

Case in an Infant] *Studii si Cercetări Inframicrobiol., Microbiol. si Parazitol.* 1957, v. 8, No. 4, 561–9, 1 diagram & 7 figs. on 4 pls. [14 refs.] French summary.

During an epidemic of influenza in Rumania in 1955 a strain of influenza virus was isolated from the intestine of an infant who had died of a fulminating attack of the disease. In inhibition tests with reference antisera the virus was shown to be of A-prime type. It could be adapted to intranasal and intracerebral passage in mice, and on primary isolation was in the O phase. The histopathological appearances in the lungs and brain of infected mice are described [the adaptation of influenza virus to mouse brain is a rare event and the observations of the authors are therefore of particular interest]. *D. J. Bauer*

FAUCONNIER, B. & BARUA, D. **Increase of Viral Haemagglutinability of Red Cells of the Mouse after Treatment with Formalin.** [Correspondence.] *Nature.* 1959, Feb. 28, v. 183, 629–30, 1 fig.

Treatment of fowl and mouse erythrocytes by formalin was shown to increase their reactivity with influenza virus haemagglutinins. Formalin-enhancement of haemagglutinability was particularly marked with mouse erythrocytes and the highest titre rises were observed with influenza B viruses. It is suggested that formalin treatment may reveal red cell receptors which normally do not react with viral haemagglutinins.
H. G. Pereira

BUCKLAND, F. E. **Impairment of Viral Haemagglutination of Red Cells after Treatment with Formalin.** [Correspondence.] *Nature.* 1959, May 2, v. 183, 1276.

The agglutinability of human group O erythrocytes by myxoviruses or by Columbia SK virus was unchanged or enhanced by formalin treatment of the cell suspensions. The same procedure caused, on the other hand, a marked reduction of haemagglutination titres obtained with adenovirus type 9 and with ECHO virus types 10 and 11. [See also FAUCONNIER and BARUA, above.]
H. G. Pereira

GOTTSCHALK, A. **On the Mechanism underlying Initiation of Influenza Virus Infection.** *Ergebn. Mikrobiol. Immunitätsf.* 1959, v. 32, 1–22, 2 diagrams. [Numerous refs.]

The interactions between influenza virus, mucoproteins and host cells are extensively reviewed and an attempt is made, with a considerable measure of success, to define some of the biochemical processes underlying the biological aspects of the problem. The action of the virus enzyme neuraminidase on substrates present in mucous secretions and on red cells is described in detail and evidence is presented demonstrating the role played by this enzyme in the processes of adsorption and penetration leading to the initiation of infection by influenza viruses. *H. G. Pereira*

NEGRONI, G. & TYRRELL, D. A. J. **Morphological Observations on Tissue Cultures of Epithelial Cells infected with Influenza-A Viruses.** *J. Path. & Bact.* 1959, Apr., v. 77, No. 2, 497–504, 9 figs. on 3 pls. [21 refs.]

Cytological alterations caused by influenza A viruses in cultures of kidney tissues are described in detail. Similar observations on mouse and monkey kidney cultures are briefly reported. The main alterations observed in virus-infected calf kidney cells consisted of reduction in the number of mitoses followed by rounding, vacuolation and fragmentation of the cells. A proportion of cells were apparently unaffected and the cultures started to regenerate at the second day after infection. The correlation between virus production and cytological alterations was investigated by means of the haemadsorption technique. *H. G. Pereira*

FROMMHAGEN, L. H. & LENNETTE, E. H. **Spontaneous Disappearance of the Slow-Sedimenting Components of Influenza Virus Preparations.** [Correspondence.] *Virology.* New York. 1959, Feb., v. 7, No. 2, 247–8, 1 fig.

Purified preparations of PR8 influenza virus were shown to contain 2 main components sedimenting at 200 to 500 S and 700 S respectively. Storage of such virus materials at 4°C. for 10–20 days or at 37°C. for 10–20 hours brought about the disappearance of the 200–500 S component with a corresponding increase of the 700 S boundary. Preparations of incomplete PR8 virus also contained the 2 components but the slow-moving component could be made to coalesce with the 700 S component only after incubation at 37°C. for 3 to 5 hours in the presence of 0·05 M sodium cyanide.

Preparations of Lee (1940), Denver (1957) and Japan 305 (1957) strains behaved similarly to PR8 but coalescence of the 2 boundaries could only be readily detected in the presence of cyanide. *H. G. Pereira*

NÁSZ, I. & TÓTH, Margit. Emberi amnion és Detroit 6 szövettenyészeteknek különböz típusú adenovírusok iránti fogékonysága és degenerációja. [**Susceptibility of Human Amnion and Detroit 6 Tissue Cultures to Adenoviruses of Several Types and their Degeneration**] *Egészségtudomány.* Budapest. 1958, v. 2, No. 3, 221–7, 10 figs. [14 refs.] English summary.

An investigation has been made of the behaviour of adenovirus of types 1–7 in cultures of Detroit-6 and human amnion cells. 2 kinds of cytopathic effect were observed in amnion cell cultures. The first kind was produced by types 3, 4 and 7 viruses; the cells became rounded and refractile and foci of degeneration appeared. The second kind of effect was observed with the remaining strains; the cells became granular and separated from each other. No difference in cytopathic effect was observed when the strains were grown in Detroit-6 cells, and the effect developed more rapidly in Detroit-6 and HeLa cells than in amnion cell cultures. *D. J. Bauer*

STEINMAN, H. G. & MURTAUGH, Patricia A. **Isoelectric Precipitation of Adenovirus and of its Complement-Fixing Antigen.** *Virology.* New York. 1959, Mar., v. 7, No. 3, 291–9, 4 figs. [14 refs.]

The isoelectric points of infective and complement-fixing factors present in adenovirus preparations was determined in media varying in ionic strength. The values obtained at low salt concentration were of 3·9 and 3·4 for virus and complement-fixing antigen respectively. At increased ionic strengths the isoelectric points were shifted to lower *p*H values. Separation of virus from complement-fixing antigen was partially achieved by differential isoelectric precipitation and by electrophoresis on paper. It is suggested that the method may be of value for the concentration and separation of the 2 components of the adenovirus complex.

A simian strain of adenovirus (M2) propagated in monkey kidney cultures was employed.

H. G. Pereira

SYVERTON, J. T. **An Appraisal of the Enterovirus Problem.** *Amer. J. Trop. Med. & Hyg.* 1959, Mar., v. 8, No. 2, Pt. 1, 101–9. [75 refs.]

This paper is a valuable review of the Enterovirus problem. The 51 Enterovirus types of man at present recognized are listed, and it is noted that similar agents have been isolated from monkeys, cattle and swine and are probably present in other species. The range of pathogenic capabilities of the group is discussed as are the epidemic propensities. The results obtained by Dr. Syverton from 1955 to 1958 in the investigation of cases of poliomyelitis and non-bacterial meningitis are summarized. In 1955 there were 218 cases of proved paralytic poliomyelitis and 292 of non-paralytic poliomyelitis. In 1956 these figures were down to 67 and 82 but 75 Coxsackie B5 isolations were made from patients with meningitis. The following year ECHO 9 virus was the major virus isolated from cases of non-bacterial meningitis and in 1958 Coxsackie B5. In this year only 2 cases of non-paralytic poliomyelitis proved virologically occurred. In both 1957 and 1958 well over 50% of the cases of meningitis were of undetermined aetiology.

A. J. Beale

INTERNATIONAL POLIOMYELITIS CONGRESS. **Poliomyelitis: Papers and Discussions presented at the Fourth International Poliomyelitis Conference** [Geneva, July 1957]. pp. xviii + 684, numerous illustrations. [Numerous refs.] 1958. Philadelphia: Montreal: J. B. Lippincott Co.

This volume contains all the papers and discussions which took place at the 4th International Poliomyelitis Conference in Geneva in July 1957. Despite the fact that this is a fast-advancing field it is of great interest, drawing together information from a wide field of study. The conference was the first to take place after the demonstration of the effectiveness of killed poliovaccine, and did so therefore in an atmosphere of confidence that at last the conquest of poliomyelitis was an imminent possibility. The first sessions dealt appropriately with poliovaccine. Pride of place was given to killed vaccine with papers by J. E. SALK (pp. 66–76), D. BODIAN (pp. 77–85) and A. D. LANGMUIR (pp. 86–92). The measures taken to produce safe vaccine after the Cutter disaster were described. This had led to a fall in potency of the vaccine, which nonetheless still appeared to be effective. The measures of effectiveness without a field trial are crude. The results of the British trial and antigenic potency of British vaccine were presented. Some of the causes of loss of potency were discussed. The second session, with papers by H. KOPROWSKI (pp. 112–23), A. B. SABIN (pp. 124–35) and J. P. FOX (pp. 136–49), was devoted to attenuated vaccine. The disadvantages of killed vaccine are poor potency, expense, doubt about the duration of immunity (although Salk presented evidence that it may be long-lasting) and the lack of an effect on alimentary carriage of virus. Attenuated vaccine may overcome these problems and be used either to replace or complement killed vaccine. Dr. A. M. M. PAYNE (pp. 157–64) introduced a discussion on the indications for poliomyelitis immunization programmes in which J. R. PAUL reiterated the view that when the infant mortality rate in a country falls to 100–75, preventive measures should be taken.

The problems of ECHO and Coxsackie viruses, opened up when tissue culture and suckling mice were used as tools for the study of poliomyelitis, were introduced by J. L. MELNICK (pp. 187–202), D. T. KARZON (pp. 203–6), G. J. DALLDORF (211–20), M. L. FURCOLOW (pp. 221–5) and J. H. S. GEAR (pp. 226–9). The role of these viruses as a cause of meningitis and other disease syndromes was stressed.

The preparation of poliomyelitis vaccine demands the use of large numbers of monkeys, and the use of a continuous cell line would help to solve the problem of the cost of the vaccine. The discussion on cultured mammalian cells was introduced by an authoritative team consisting of H. EAGLE (pp. 244–5), T. T. PUCK (pp. 248–56), R. C. PARKER (pp. 257–67) and, to discuss malignancy, A. E. MOORE (pp. 268–76). Additional interesting papers on nutritional aspects were given by CHANG and MELNICK. The problem of malignancy of continuous cell lines and their mode of origin remained unsolved.

2 sessions were devoted to general virus problems. G. SCHRAMM (pp. 294–7) discussed his and H. L. FRAENKEL-CONRAT's outstanding work on the nucleic acid components of tobacco mosaic virus. C. E. SCHWERDT (pp. 298–305) described the crystallization of poliovirus, and R. C. WILLIAMS (pp. 306–14) and C. MORGAN (pp. 315–24), electron microscopy. The second session about virus multiplication, latency and genetics was introduced by F. M. BURNET (p. 334), who explained the quandary as to whether it was possible to generalize about viruses or whether the differences between them were too great despite the methodology that grouped them together. M. DELBRÜCK (pp. 342–53), in an excellent discussion of virus genetics, agreed by limiting himself to phage genetics mainly on the grounds that phage contains DNA whereas many animal and plant viruses contain RNA. However, all phages were embraced in his discussion. Other papers were by F. L. HORSFALL (pp. 335–40), T. FRANCIS (pp. 361–5) and Kenneth M. SMITH (pp. 354–60).

The next session was on diagnosis which started with a comprehensive discussion of the laboratory diagnosis by E. H. LENNETTE (pp. 377–86). A. B. SABIN (pp. 387–8) discussed problems of virus isolation. MELNICK (pp. 394–7), discussed the complement-fixation test. He and later speakers pointed out that cross-reactions between various Enteroviruses may limit the specific value of the complement-fixation test. G. L. LE BOUVIER (pp. 392–3) and G. CHURCHER (pp. 398–9) discussed various aspects of the precipitin test. SALK (pp. 389–91) discussed the neutralization test as a means of detecting immunity. M. K. VOROSHILOVA in a discussion of laboratory diagnosis of poliomyelitis described the isolation of the Russian Coxsackie A7 originally thought to be poliovirus Type 4.

The remaining sessions were devoted to the problems associated with the care of severe cases of poliomyelitis. The striking advances that have been made in this field were fully discussed and described. The importance of mental, emotional and individual aspects of the care of poliomyelitis patients is stressed.

These papers are well worth reading and the volume is particularly valuable in luring the clinician to read papers on virology and vice versa. *A. J. Beale*

PRIER, J. E. & SULLIVAN, R. **Development of a Chick Embryo Heart Cell for the Cultivation of Poliovirus.** *Science.* 1959, Apr. 17, v. 129, 1025–6, 2 figs. [11 refs.]

Since the discovery that the continuous embryo rabbit kidney cell line developed by WESTWOOD *et al.* [this *Bulletin*, 1957, v. 32, 815] was sensitive to poliovirus [SHEFFIELD and CHURCHER, *ibid.*, 1957, v. 32, 816] and that these cells share common antigens with HeLa and other continuous cell lines (MELNICK and HABEL, *Federation Proc.*, 1958, v. 17, 526) there has been a tendency to explain the observations as contamination of the cells in the laboratory. More recently a continuous guineapig spleen cell sensitive to poliovirus has been described [MASCOLI *et al.*, this *Bulletin*, 1959, v. 34, 833] and now a chick embryo heart cell also sensitive to the 3 types of poliovirus is described. Care was taken to avoid contamination by carrying out trypsinization procedures in an area not used for other cell cultures. Cells were propagated in 10% calf serum in medium 199. The first 4 passages contained mainly fibroblast-like cells, but by the 6th passage these were almost entirely replaced by "epithelial" cells. Cells from the first passage were insensitive to poliovirus, whereas from the 6th passage they were sensitive yielding $10^{-5\cdot6}$, $10^{-5\cdot5}$, $10^{-5\cdot2}$ for TCD50 for Types 1, 2 and 3 respectively. The early passage strains insensitive to poliovirous did not contain the common cell line complement-fixing antigen, but the later epithelial type passage strains sensitive to poliovirus did contain this antigen. *A. J. Beale*

MCLAREN, L. C.; HOLLAND, J. J.; SYVERTON, J. T. **The Mammalian Cell-Virus Relationship. I. Attachment of Poliovirus to Cultivated Cells of Primate and Non-Primate Origin** [MCLAREN, HOLLAND & SYVERTON]. *J. Exper. Med.* 1959, May 1, v. 109, No. 5, 475–85, 2 figs. [24 refs.]

II. Adsorption, Reception, and Eclipse of Poliovirus by HeLa Cells [HOLLAND & MCLAREN]. *Ibid.*, 487–504, 2 figs. [30 refs.] **III. Poliovirus Production by Non-primate Cells exposed to Poliovirus Ribonucleic Acid** [HOLLAND, MCLAREN & SYVERTON]. *Proc. Soc. Exper. Biol. & Med.* 1959, Apr., v. 100, No. 4, 843–5.

These 3 important papers describe what happens when cultivated cells of primate or non-primate origin are infected with intact poliovirus or with the ribonucleic acid derived therefrom.

(I) After 2 hours at 37°C. over 90% of the poliovirus was adsorbed by a variety of continuous cell lines and primary cells of human or monkey origin which showed a cytopathic effect after poliovirus infection. By contrast less than 10% of virus was adsorbed by a similarly large variety of primary and continuous cells derived from non-primates, particularly dog, cat, swine, calf, guineapig, mouse, chick and rabbit. There was one exception to this rule and that was the ERK 1 cells described by WESTWOOD *et al.* [this *Bulletin*, 1957, v. 32, 815]. These cells are known to be sensitive to poliovirus and they adsorbed 90% of the infecting virus in 2 hours at 37°C. Disruption of susceptible cells revealed that most of the adsorbed virus was not recoverable, *i.e.* that an eclipse phase had occurred. Approximately 1–3% of the adsorbed virus was recoverable by disruption of the cells and a similar proportion of cell associated virus could be recovered from non-susceptible cells. This cell associated virus eluted continuously from non-susceptible cells so that after 40 hours only about 10% of it remained cell associated. Virus eluted from cells was not altered in its character.

(II) In the second paper the early stages of infection of HeLa cells with poliovirus are described. Virus adsorbed to cells could not be eluted with 0·25 M sucrose or 0·1 M calcium chloride. Adsorption of virus was reduced but not prevented by the absence of ions or by the presence of high cation concentrations. This effect was more marked with cell suspensions than monolayer sheets. Adsorption by cell monolayers was 10-fold less at 1°C. than at 37°C. but only 2-fold less with suspended cells. Adsorbed virus was initially sensitive to specific antiserum but at 37°C. rapidly disappeared beyond the reach of antiserum. The penetration of virus into the cell was not affected by ribonuclease or by various anticellular agents (metabolic inhibitors, cytotoxic antiserum and Tween 80). Virus was not recoverable from infected cells. Viral eclipse did not require the presence of viable host cells but appeared to be mediated by a lipoprotein of the cell wall. Thus cell debris obtained by freezing and thawing inactivated virus and this capacity of cell debris was destroyed by trypsin and by ether or chloroform. Also cell debris derived from insusceptible non-primate cells did not inactivate poliovirus. Ether treatment or sonic disruption of virus inactivated by cell debris yielded only a small proportion of the inactivated virus suggesting that the virus was not merely bound to some receptor site but actually changed in chemical or physical state.

(III) In the third paper the effect of treating susceptible and non-susceptible cells with ribonucleic acid

extracted from poliovirus by the method of GIERER and SCHRAMM (*Ztschr. f. Naturforsch.*, 1956, v. 11b, 138), is described. The observations of ALEXANDER *et al.* [this *Bulletin*, 1959, v. 34, 177] showing that ribonucleic acid from poliovirus induces the formation of infectious poliovirus and cytopathic effects in susceptible cells was confirmed. Ribonuclease, which has no effect on intact virus, destroys the infectivity of RNA preparations. Virus accumulated in the cells before being released into the culture fluid as occurs after infection with intact virus. When non-susceptible cells of non-primate origin either in Maitland type cultures or in monolayer cultures of either primary or continuous cells were infected with poliovirus RNA fully infectious intact virus accumulated in the culture fluids in similar amounts and time sequence to that formed in susceptible cells, although there was no cytopathic effect upon the non-primate cells. Similarly, after intracerebral inoculation of viral RNA into mice, rabbits, guineapigs, chicks or hamsters poliovirus was detected in the brains 18 or 36 hours after infection.

[These 3 most important papers should be read in the original.] *A. J. Beale*

DUNNEBACKE, T. H. **The Yield of Poliovirus from Individual Cells in Tissue Culture.** [Correspondence.] *Virology*. New York. 1959, Feb., v. 7, No. 2, 243–6.

The yield of poliovirus from isolated single cells of monkey kidney or human amnion cultures, or a variety of cell lines, was determined. With monkey cells it was found that the yield of poliovirus from cells of the same size was about 1·7 times greater for Mahoney strain of Type 1 than for the Saukett strain of Type 3. The MEF 1 strain gave intermediate yields. The yields were greater from bigger cells. Although the yields varied from experiment to experiment there was no evidence that the yield for Mahoney Type 1 varied significantly in the different types of cell. *A. J. Beale*

HOYER, B. H., BOLTON, E. T., RITTER, D. B. & RIBI, E. **Simple Method for Preparation of Purified Radioactive Poliovirus Particles: Electron Micrograph.** [Correspondence.] *Virology*. New York. 1959, Apr., v. 7, No. 4, 462–4, 1 fig.

A method for preparing highly purified preparations of radio-active poliovirus particles is described and its effectiveness depicted in a striking illustration. This simple method can be carried out on 100–600 ml. of virus. Monkey kidney cells were grown in medium containing 0·001 M citrate instead of phosphate, subsequently they were infected with a large dose of poliovirus (type 2, Lansing strain). After virus adsorption the medium was changed to one containing 0·013 mc. of ^{32}P orthophosphate per ml. for every million monkey kidney cells. 48 hours later the cultures were frozen and thawed and the cell debris removed by spinning at 1,000 g for 20 minutes. The virus was then deposited at 80,000 g for 90 minutes and the pellet resuspended in a small quantity of 0·02 M phosphate buffer. The titre of virus at this stage was about $4{\cdot}4 \times 10^{10}$ PFU per ml. The virus was then added to a DEAE column and washed through with more 0·02 M phosphate buffer. The runnings from the column which contained the first peak of radio-activity were pooled and contained the great majority of the infectious virus. After centrifugation at 100,000 g for 90 minutes and resuspension of the deposit in distilled water, electron microscope pictures showed the virus to be embedded in a homogenous layer of very fine particles. The supernatant following further centrifugation at 10,000 g for 20 minutes was found to contain virus of similar purity to that obtained by SCHWERDT and SCHAEFFER (*Ann. N.Y. Acad. Sci.*, 1955, v. 61, 740). *A. J. Beale*

ACKERMANN, W. W., LOH, P. C. & PAYNE, F. E. **Studies of the Biosynthesis of Protein and Ribonucleic Acid in HeLa Cells infected with Poliovirus.** *Virology*. New York. 1959, Feb., v. 7, No. 2, 170–83, 1 fig. [19 refs.]

The amounts of protein, RNA (and rate of incorporation of ^{32}P) DNA and virus in HeLa cell fractions were determined at intervals after infection (at a multiplicity of about 100) with Type 1 poliovirus (Mahoney strain). It was found that protein and RNA started to accumulate in the cytoplasm immediately after infection. Virus appeared in the cells at 3 hours and rapidly increased till 7 hours when virtually all the yield of virus was present in the cell. Evidence (mainly from the nucleotide base ratios) suggests that most of the RNA and protein appearing in the cell after virus infection is not destined to be incorporated in virus.
A. J. Beale

i. LÉPINE, P. A propos des vaccins et vaccinations contre la poliomyélite. [**Poliomyelitis Vaccines and Vaccinations**] *Rev. d'Immunologie*. 1959, Jan.–Mar., v. 23, Nos. 1/2, 1–14. [Refs. in footnotes.]

ii. RAMON, G. Vaccins et vaccinations contre la poliomyélite. [**Poliomyelitis Vaccines and Vaccinations**] *Ibid.*, 15–30. [Refs. in footnotes.]

i. Ramon in an earlier paper [this *Bulletin*, 1959, v. 34, 420] criticized the haste with which poliomyelitis vaccine has been put into large-scale use. He compared the long, careful and painstaking work which went into the elaboration and perfection of diphtheria prophylactics before their mass use with the publicity and sensationalism that ushered in poliovaccine. The same slow but sure methods should have been employed for poliovaccine rather than allowing the mass use of inadequately proved vaccine. Lépine has jumped to the defence of killed vaccine and particularly to the policy and achievements of the French in the field. While admitting that the vaccine is far from perfect he believes that it provides a worthwhile measure of protection. Efforts are being made to enhance potency, to improve dosage schedule and to combine poliovaccine with other prophylactics. French poliovaccine differs from that produced elsewhere, in the strains employed (which are partially attenuated), and in the inactivating agents which are formalin with the addition of β propiolactone; also the inactivation is done at 4°C. and lasts only 3 days and only a relatively coarse

filtration is used. Safety tests are done only in tissue cultures and potency is assessed in chickens. Up to the end of October 1958 over 2 million doses of this vaccine have been used by the Pasteur Institute in France. The evidence is reviewed that immunity to poliomyelitis cannot be interpreted solely in terms of neutralizing antibody levels. Mainly for this reason Lépine considers that a comparison between poliovaccine and diphtheria or tetanus toxoids is invalid. However, since there is no other measure available he believes neutralizing antibodies have to be used as a guide to the immune status. Serological studies with French vaccine are briefly reviewed. In triple negative children, after 2 doses of vaccine 90% developed Type 1 antibodies although only 37% developed antibodies to all 3 types.

ii. Ramon, in the following paper, reiterates his view that those responsible for the poliovaccine programme should proceed with caution in the mass use of poliovaccine. This vaccine in his view has not reached in either its killed or attenuated state the perfection achieved by diphtheria toxoid. It would in his view be better to concentrate on improving the vaccine rather than using it in its present imperfect state.

A. J. Beale

KOPROWSKI, H. **Live Poliomyelitis Vaccine.** [Correspondence] *Brit. Med. J.* 1959, May 23, 1349–50.

This letter contains sharp criticism of Dr. SABIN'S recent account of the position of attenuated poliovaccine [this *Bulletin*, 1959, v. 34, 835]. Sabin asserted that the vaccine used by Koprowski (in the Belgian Congo) contained an unidentified virus besides poliovirus. This is denied, tests in 2 laboratories besides Koprowski's are said to have failed to find this agent, and the powerful polio antiserum by which Sabin uncovered the virus was not made available to Koprowski. Similarly, he complains of lack of cooperation from Sabin in the exchange of strains. The results of intraspinal and intracerebral inoculation of the Chat strain obtained by Koprowski's and 4 other laboratories are presented. These are in marked contrast to the results obtained by Sabin, whereas from Sabin's results the intraspinal infectivity was calculated at greater than 10^{-5}, the titre from the combined results of the other 5 laboratories is less than 10^{-1}. Sabin's view elaborated in his paper [*loc. cit.*] that the discrepancy is due to technical details of the intraspinal inoculation is rejected. Sabin reported privately that the paralysis was non-progressive and developed within 2–4 days in all but 1 animal. Koprowski asserts that paralysis has not been observed in his laboratory after a dose of 100 TCD50 [this is less than that employed in the majority of Sabin's tests] in under 4 days. Koprowski alleges that MELNICK (*Proc. Soc. Exper. Biol. & Med.*, in press) has evidence that Sabin's L Sc and P 712 strains are of comparable pathogenicity to the Brunhilde-Enders strain by the intraspinal route. Finally a plea is made for evaluating attenuated vaccines on performance rather than personalities.

[Too much of the work on attenuated poliovaccines has been circulated as confidential memoranda. There has also been a distressing lack of reproducibility of the results, *cf.* the failure of DANE *et al.* (*ibid.*, 1957, v. 32, 311) to confirm Koprowski's findings and that of CLARKE *et al.* (*ibid.*, 1959, v. 34, 201) to confirm Sabin's. More work is required—or more should be published—in order to put attenuated poliovaccine on a sound footing.]

A. J. Beale

PONTECORVO, M. Richerche sperimentali sulla risposta sierologica al vaccino antipoliomielitico associato ad altri antigeni. [**Experimental Studies on the Serological Response of Poliomyelitis Vaccine Associated with Other Antigens**] *Riv. Istituto Sieroterap. Ital.* 1959, Mar.–Apr., v. 34, No. 2, 81–7. [17 refs.]

The English summary appended to the paper is as follows:—

"The present study reports the serological response of guinea-pigs and mice to combined diphtheria-pertussis and poliomyelitis vaccines (DPP) in comparison with DP and poliomyelitis vaccines given individually.

"The guinea-pigs were given subcutaneous injections of DP, poliomyelitis and combined vaccines (DPP) according to the Gard schedule. Mice were given subcutaneous injections of DP and DPP vaccines according to the Evans and Perkins schedule. The immunogenic capacity of poliomyelitis is recorded as antigenic extinction limit titres in log units (table 3); the diphtheria antitoxin and the pertussis agglutinins as geometric mean titre of individual levels (table 4 and 5).

"The poliomyelitis antibody response was not lowered by the presence of diphtheria and pertussis antigens and the antigenicity levels appeared to be higher following the combined product containing aluminum phosphate 1 mg per ml than following poliomyelitis vaccine alone or plain combined product. Pertussis and diphtheria antibodies reached approximately equal levels from the DP and DPP vaccines aluminum phosphate adsorbed."

HSIUNG, G. D. **Effect of X-Irradiation on Patas Monkey Kidney Cell susceptibility to Enteroviruses.** *Virology.* New York. 1959, Feb., v. 7, No. 2, 140–49. [13 refs.]

Coxsackie A9 virus grows well in kidney cells from rhesus monkeys but poorly in those from patas monkeys. Sometimes small plaques appear on patas cells after large doses, but on serial transfer or prolonged incubation virus is gradually eliminated though at a much slower rate than from medium alone at 37°C. and a slightly slower rate than from dead cultures. Irradiation of the cultures (210 r within 24–48 hours of seeding from primary and 14 hours for second generation cells) allowed greater multiplication of Coxsackie A9 virus and by the 5th serial passage marked cytopathic changes were observed. Patas cultures infected with Coxsackie A9 and appearing normal were still sensitive to poliovirus (Mahoney strain) whether the cultures had been irradiated or not. After 14 passages in irradiated cells the virus produced cytopathic effects and plaques in nonirradiated cells. It was antigenically unchanged but was less pathogenic for suckling mice. Irradiation of older cultures (7–14 days) was ineffective even with 100 times the dose. Irradiation produced giant cells 10 or

more days after treatment but it was not established whether viral multiplication took place preferentially in these as has been reported for Newcastle disease virus (Cieciura *et al.*, *Virology*, 1957, v. 3, 426). Similar attempts were made to adapt ECHO 1, 6 and 9 viruses to patas kidney cells. These were unsuccessful with ECHO 6 and 9. ECHO 1 virus produced cytopathic effects in irradiated cells after 3 serial passages. The virus titre was also higher in irradiated cultures, but unlike Coxsackie A9, ECHO 1 virus persisted through at least 10 serial passages in unirradiated cells.

A. J. Beale

Albrecht, P. & Mayer, V. **A Comparison of Tissue Affinity in Two Type B1 Coxsackie Viruses and the Relationship of the Virus to the Parotid Glands in White Mice.** *Acta Virologica.* Prague. 1958, Oct.–Dec., v. 2, No. 4, 245–9.

The histological features of Coxsackie B1 virus in suckling mice was studied using 2 strains of the virus Bučič and Klíč. Bučič strain produced parotitis in addition to lesions in liver, pancreas and adipose tissue. A substrain of Bučič isolated and maintained in HeLa cells did not cause parotitis, nor did the Klíč strain. The Conn-5 strain of Coxsackie B1 at its 40th suckling mouse passage by the subcutaneous route only showed lesions in the central nervous system and adipose tissue lesions in myocardium, skeletal muscles, liver and pancreas were not observed. The observation of parotitis in mice infected with the Bučič strain is thought to lend force to the report by Howlett *et al.* (*Canad. Med. Assoc. J.*, 1957, v. 77, 5) of the isolation of Coxsackie A virus from 4 patients with herpangina and parotitis not due to mumps.

A. J. Beale

Smith, L. W. & Cheever, F. S. **Relation of Viral Proliferation and Antibody Formation in Mice exposed to Roentgen Radiation.** *Proc. Soc. Exper. Biol. & Med.* 1959, Apr., v. 100, No. 4, 817–20. [10 refs.]

"1. X-radiation administered prior to Coxsackie virus inoculation increased and prolonged the yield of virus from selected tissues, particularly the pancreas. 2. X-radiation administered prior to virus inoculation inhibited the specific immune response. 3. The deleterious effects of irradiation on antibody formation were not long lasting, in that virus reinoculated 30 days after x-ray exposure evoked a prompt secondary response equal to that of control mice. 4. X-radiation exposure prior to a second inoculation of virus inhibited the secondary response in both the previously irradiated and control mice. 5. These data are compatible with the hypothesis that increased viral proliferation in X-radiated animals is due to the inhibition of the antibody response."

Lycke, E., Hultgardh, A. & Redin, B. **Coxsackie B1 Virus and Febrile Illness with Rash.** [Correspondence.] *Lancet.* 1959, May, 23, 1097.

Coxsackie B1 was isolated from the stools of a 9-month-old boy who suffered from a febrile disease with a rubella-like rash. There was a rise in Coxsackie B1 neutralizing antibodies from 1/128 to 1/512 and it is concluded that Coxsackie B1 should be added to the growing list of enteroviruses capable of causing a rubella-like rash. The Coxsackie B1 was isolated in HeLa and monkey kidney cells but was not pathogenic for suckling mice on primary isolation. Attempts to find another enterovirus in the stool specimen by the use of Coxsackie B1 antiserum failed.

A. J. Beale

Fukumi, H., Nishikawa, F. & Mizutani, H. **Further Studies on the 57–67 Virus.** *Japanese J. Med. Sci. & Biol.* 1958, Dec., v. 11, No. 6, 461–5, 1 fig.

A virus isolated from a patient suffering from upper respiratory infection [56–67 virus, Fukumi *et al.*, this *Bulletin*, 1959, v. 34, 293] and having some properties of enteroviruses was compared with ECHO viruses by serum neutralization tests in HeLa cell cultures. The results show that the 57–67 virus is antigenically related to ECHO 6 and to a lesser extent to ECHO 1. It differs from ECHO viruses, however, in its failure to multiply in monkey kidney cultures and its lack of haemagglutinating activity.

The cytopathic effect of the 57–67 virus was incomplete. Surviving cells from infected cultures were subcultured and shown to be insusceptible to reinfection by 57–67 virus or by ECHO virus while maintaining full susceptibility to Coxsackie B and adenoviruses.

Antibodies for the 57–67 virus were found to be widely distributed in several communities.

H. G. Pereira

Trinidad. **Annual Report of the Trinidad Regional Virus Laboratory, January 1st–December 31st 1958.** 144 mimeographed pp. 1959. Port-of-Spain: West Indies.

This is a detailed and valuable account of 5 years' work directed mainly to the elucidation of the distribution, epidemiology, and animal reservoirs of arboviruses in the West Indies. Investigations were also made of some aspects of other virus infections (rabies, Newcastle disease, poliomyelitis, and influenza) and of several non-viral infections (toxoplasmosis, histoplasmosis, trypanosomiasis, and leptospirosis). Widespread serum antibody surveys were used and the use of sentinel animals is described. A great deal of ornithological study was carried out including experimental infections of birds with some of the arboviruses isolated. Entomological studies included biological studies in addition to attempts to isolate viruses from haematophagous insects. The Report reviews the haematophagous arthropod fauna of the area. Viruses were isolated from a variety of sources and 19 designated as prototypes are fully described. This is the story of a remarkable study of virus and other problems in the West Indies and should be read in full.

C. E. Gordon Smith

Porterfield, J. S. **Plaque Production with Yellow Fever and Related Arthropod-Borne Viruses.** [Correspondence.] *Nature.* 1959, Apr. 11, v. 183, 1069–70.

Monolayers of chick fibroblasts grown by overnight incubation of 40–50 $\times$ 10^6 cells in 5 ml. of medium,

were infected then overlaid. Cells remained healthy for 7 or more days with the media used. 17D yellow fever virus containing 8×10^6 mouse LD50 per ml. gave titres of $1{\cdot}4 \times 10^6$ to $4{\cdot}5 \times 10^6$ plaque-forming units per ml., the plaques being 2–3 mm. in diameter on or after the 4th day. Uganda S, West Nile, Wesselsbron, and Japanese encephalitis viruses gave plaques on the second or third days, increasing in size to about 5 mm. Zika behaved like 17D virus. French neurotropic yellow fever virus gave larger plaques than 17D. Louping ill virus gave less definite plaques 2–3 mm. in diameter. The plaques formed by all these viruses were less clearly defined than those of western equine encephalomyelitis virus but the nature of the difference has not yet been determined. *C. E. Gordon Smith*

Traub, E. Über den Verlauf der Infektion mit dem EEE-Virus und die Entwicklung der aktiven Immunität bei erwachsenen Mäusen. [**The Course of Infection with EEE Virus and the Development of Immunity in Adult Mice**] *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 173, Nos. 5/6, 330–44. [18 refs.]

In mice infected subcutaneously with eastern equine encephalomyelitis virus, viraemia could be demonstrated after 6 hours and the primary site of multiplication was apparently in the bone marrow, and possibly also in the regional lymph nodes, liver and ovaries. Viraemia passed off after 12–24 hours, and the virus could then be found in the spleen, kidneys and central nervous system. At the time of appearance of symptoms 72 hours after infection virus was present in the central nervous system in titres ranging up to 8 log units. Neutralizing antibody appeared in the spleen 3 days and in the serum 4 days after infection, and could subsequently be found in the lymph nodes, liver and ovaries. Immunity to intracerebral challenge infection appeared after 5 days. *D. J. Bauer*

Ada, G. L. & Anderson, S. G. **Yield of Infective "Ribonucleic Acid" from Impure Murray Valley Encephalitis Virus after Different Treatments.** *Nature.* 1959, Mar. 21, v. 183, 799–800, 2 figs.

Infective ribonucleic acid (RNA) was prepared by phenol extraction of baby mouse brain infected with Murray Valley encephalitis virus. Infectivity was destroyed by ribonuclease and by normal rabbit serum but was stable in saline. Infectivity was assayed on the chorio-allantoic membrane of chick embryos.

Treatment of a crude brain suspension with 9% phenol completely removed its infectivity, which was restored to about 1/100th of its initial level by completing the extraction process with 90% phenol. When the infectivity of crude material was destroyed by heating to 56°C. or 62°C. phenol extraction yielded RNA titring 10^{-2} or more. Similarly from crude material which had been exposed to a *p*H of 2 or 3, thus reducing its infectivity more than 1,000-fold, phenol extraction gave material of higher infectivity than after acid treatment.

The infectivity of material treated with formalin could not, however, be increased by phenol extraction and the authors therefore suggest that while phenol, heat, and acid *p*H denature the surface protein of the virus leaving the RNA intact, formalin affects the RNA itself. *C. E. Gordon Smith*

Vagzhanova, V. A. **The Effect of Tick-Borne Spring-Summer Encephalitis Virus on Development of Ehrlich's Ascitic Carcinoma.** Preliminary Report. *Acta Virologica.* Prague. 1959, Apr., v. 3, No. 2, 101–4. [12 refs.]

"1. Tick-borne encephalitis virus strain Yam-3 and Ukh-10, administered intraperitoneally to mice in a mixture with Ehrlich's ascitic carcinoma, inhibited the development of latter.

"2. Experiments in chick embryos did not reveal the oncolytic activity of viruses because of the high mortality of embryos resulting from normal tumour development and prolonged virus incubation."

Kovac, W. & Moritsch, H. Zur Pathogenese der Infektion der Maus mit dem Virus der menschlichen Frühsommer - Meningoencephalitis. 1. Vergleichende virologisch-histologische Untersuchungen. [**Pathogenesis of the Infection of Mice with the Virus of Human Spring-Summer Meningoencephalitis. 1. Comparative Virological and Histological Investigations**] *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 174, Nos. 5/6, 440–56, 15 figs.

Mice were infected subcutaneously with spring-summer meningoencephalitis virus and the content of virus in various organs and the corresponding histological appearances were investigated in groups of animals each day over a period of 6 days after infection. Virus was found in the blood over the whole period; the titre in the brain rose steadily to attain 10^8 on the 6th day, whereas the titre in the liver and spleen pursued a biphasic course with a minimum on the 3rd day and maxima of less than 10^3. The histological findings in the organs are described and illustrated in detail, and form the main part of the paper. The extent and general distribution of the lesions corresponded in general to the amount of virus found in the organs. The authors conclude that the infection occurs in 2 phases; (1) multiplication in the liver and spleen, followed by (2) multiplication in the central nervous system, beginning on the 4th day [the titration curve presented shows that multiplication of the virus in the central nervous system is already in progress on the first day]. *D. J. Bauer*

Streissle, G. Virämie bei Küken nach subcutaner Infektion mit dem Virus der Zeckenencephalitis. [**Viraemia in Chickens after Subcutaneous Infection with Tick-borne Encephalitis Virus**] *Ztschr. f. Hyg. u. Infektionskr.* 1958, v. 145, No. 4, 331–4.

8–10-day-old chickens were infected subcutaneously with 10^4 LD50 of the mouse-adapted X strain of tick-borne encephalitis virus, and blood was withdrawn at

daily intervals and titrated intracerebrally in mice in order to investigate the occurrence of viraemia. No signs of illness were observed in the chickens, but virus could be found in the blood on the 1st or 2nd day after infection, rising to a maximum titre of 4–5 log units on the 3rd–4th day and disappearing by the 7th day. Viraemia could also be demonstrated when the infecting dose of virus was as low as 16 mouse LD50.

D. J. Bauer

Boulger, L. R. & Porterfield, J. S. **Isolation of a Virus from Nigerian Fruit Bats.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1958, Sept., v. 52, No. 5, 421–4.

In attempts to detect the presence of rabies virus among fruit bats (*Eidolon helvum*) in Lagos by the intracerebral inoculation of mice a new virus was recovered from the pooled brains of 6 bats from a total of 42 animals examined. The virus could be maintained through 8 intracerebral passages, during which the survival time fell from 14·8 to 7·2 days and the titre increased from 4·2 to 5·3 log units. The virus was not pathogenic for adult mice on subcutaneous or intraperitoneal inoculation, but was pathogenic for 4-day-old mice by all 3 routes; no signs of illness were observed in 2 guineapigs, 2 rabbits and a white collared mangabey (*Cercocebus torquatus torquatus*). The virus was not neutralized by rabies immune serum, and showed no relationship to 37 other neurotropic viruses in cross-fixation or neutralization tests.

It was considered to be a hitherto unknown virus and was named Lagos bat virus. *D. J. Bauer*

Bonciu, C., Dincolesco, M. & Petrovici, Monica. Contribution à l'étude de la maladie d'Armstrong chez la souris blanche. [**Contribution to the Study of Armstrong's Disease in White Mice**] *Arch. Roumaines Path. Expér. et Microbiol.* 1958, Sept.–Dec., v. 17, Nos. 3/4, 455–70, 16 figs. [19 refs.]

Nossal, G. J. V. **Antibody Production by Single Cells: II. The Difference between Primary and Secondary Response.** *Brit. J. Exper. Path.* 1959, Apr.; v. 40, No. 2, 118–24, 2 figs. [11 refs.]

Rats were immunized into the foot pad with a preparation of flagella from Salmonella Adelaide. In the study of primary antibody response to this antigen rats were killed 7 days after a single injection; in the study of secondary response rats were killed 6 days after a second injection 4–6 weeks after the first. Single cells from the popliteal lymph nodes draining the injection sites were isolated by micro-manipulation and placed in drops of nutrient fluid under a layer of paraffin oil. After incubation of the drops at 37°C. for 4 hours antibody released by the cell into the drop was determined by introducing 7–10 motile Salm. Adelaide and observing if motility was inhibited. The amount of antibody in the drop was estimated by observing the number of lots of 7–10 organisms introduced at 30-minute intervals which were rendered non-motile.

Of 662 cells from rats showing a primary response 2·3% formed antibody, and of 214 cells from animals showing a secondary response 14% formed antibody. Cells showing a secondary response formed on average 1·7 times as much antibody as cells showing a primary response.

The author concludes that the most important difference between the secondary and the primary response to an antigen is that in the secondary a much larger proportion of cells actively form antibody.

[For earlier studies by the author, see this *Bulletin*, 1959, v. 34, 403.] *I. B. R. Duncan*

Bridges, R. A., Condie, R. M., Zak, S. J. & Good, R. A. **The Morphologic Basis of Antibody Formation Development during the Neonatal Period.** *J. Lab. & Clin. Med.* 1959, Mar., v. 53, No. 3, 331–57, 12 figs. [38 refs.]

The main part of this paper reports the changes in the gamma globulin level of the serum, the efficiency of antibody formation, and the cytology of the lymph nodes, from birth until 14 months of age in a normal child whose mother suffered from acquired agammaglobulinaemia. Electrophoresis of the mother's serum during pregnancy showed no detectable gamma globulin. The infant was given injections of TAB vaccine on the second day of life, weekly for the first 2 months, and monthly for the rest of the first year, and specimens of serum examined for the corresponding agglutinins at intervals until 2 years of age.

At birth the infant's serum showed no gamma globulin peak on electrophoresis and the gamma globulin as determined by an immunological method was 11 mgm. per 100 ml., the same as the mother's. This level remained constant until 6 weeks when there was a rise to 115 mgm. per 100 ml. followed by a rapid rise to the levels normal for infancy. Gamma globulin was first detected by paper electrophoresis in the 10th week of life. At the 10th week also, circulating antibodies to TAB vaccine were first detected. The infant was of blood group O; the normal anti-A agglutinins appeared at 3 months and anti-B at 6 months. Lymph nodes excised at birth and at 6 days contained no plasma cells. At 3 months an excised node showed plasma cells in normal numbers, and one removed at 14 months just after an injection of TAB showed very numerous plasma cells. The authors remark that for the first 6 weeks the child was indistinguishable from a case of congenital agammaglobulinaemia, and that by 3 months it was immunologically normal in every way.

Further investigations were done to ascertain the number of plasma cells in the tissues of infants not presenting any immunological abnormality. Of 20 infants under 5 days of age none showed plasma cells in smears of bone marrow. Sections and smears of appendix and ileal wall were made from post-mortem material from young children. Of 15 infants under 1 month only one showed plasma cells and these were scanty. At 3 months most had plasma cells and at 6 months plasma cells were present in all.

The last part of the work was an investigation of antibody formation and plasma cell development in rabbits Normal rabbits of various ages were killed

and their lymph nodes examined. In rabbits aged 19 days plasma cells were seen in small numbers in only 1 of 5 and in 33-day-old animals in 2 of 4. By 61 days all the rabbits had plasma cells. Other rabbits were injected at intervals from birth with bovine serum albumin or this antigen with Freund's adjuvant. Rabbits given the antigen alone first showed plasma cells in lymph nodes and circulating antibody at 33 days. The animals receiving antigen plus adjuvant showed plasma cell proliferation at 16 days and circulating antibody was first detected at 19 days.

I. B. R. Duncan

CIUCĂ, M. Contribution à l'étude de l'immunisation anti-typhoïdique. [**Contributions to the Study of the Mechanism of Antityphoid Immunity**] *Arch. Roumaines Path. Expér. et Microbiol.* 1958, Sept.–Dec., v. 17, Nos. 3/4, 321–58, 5 text figs. & 7 coloured figs. on 7 pls. [106 refs.]

This paper is chiefly concerned with a comparison of the various antibody responses in man and the rabbit to hyperimmunization with TAB vaccine. The human sera were obtained from a series of patients with either GPI or syphilis of the nervous system who had received intravenous TAB and malarial therapy. Sera were also obtained from typhoid convalescents and those with a less recent history of typhoid fever. The immunized subjects had received 8–15 intravenous injections of a heat-killed phenolized TAB totalling up to $22{\cdot}5 \times 10^9$ organisms; the rabbits were given a series of intravenous injections of the same vaccine up to a total of $12{\cdot}5 \times 10^9$ organisms. The sera were tested for H and O agglutinins for T, A and B, TVi agglutinins, TVi complement-fixing antibodies and passive mouse protection against an intraperitoneal challenge of 100 million *Salmonella typhi* Ty 2.

There appeared to be no parallelism between the various antibody levels neither could these be related to the dose of vaccine administered. In spite of the fact that phenolized vaccine, which is known to depress Vi antigenicity, was used there were several examples of relatively high Vi agglutinin titres, but these were not paralleled in the levels of Vi complement-fixing antibody.

The author discusses the irregular results obtained in the various investigations undertaken and concludes that of all the immunity tests the mouse passive protection test is the most satisfactory and is more in keeping with epidemiological and clinical evidence. While this may well be true it seems doubtful if the test has really given us a reliable method of assessing immunity to typhoid infections unless each test is strictly controlled. It is a time consuming and very exacting test and even when all the conditions have been satisfied conflicting results are not uncommon. *H. J. Bensted*

BARNES, Joan M. **Antitoxin Transfer from Mother to Foetus in the Guinea-Pig.** *J. Path. & Bact.* 1959, Apr., v. 77, No. 2, 371–80, 2 figs. [25 refs.]

The transfer of antitoxin from mother to foetus was studied in pregnant guineapigs. Animals immunized with diphtheria toxoid several months before mating had high, stable, antitoxin titres and the ratio of foetal to maternal serum-antitoxin concentration increased rapidly from the 35th to the 63rd day of gestation. If the mother was immunized after the 46th day of gestation, neither foetal nor maternal sera contained any detectable antitoxin at birth. The route of transfer of antitoxin was followed by injecting homologous (diphtheria) and heterologous (horse tetanus) antitoxin into the uterine lumen about the 44th, 55th and 63rd days of gestation. Both homologous and heterologous antitoxin were detected in foetal serum 24 hours later. Further experiments were carried out to see whether absorption was by way of the foetal gut or the vitelline blood vessels. Diphtheria antitoxin injected into the foetal stomach was not found in the foetal serum. On the other hand, if the mother was injected intracardially and the vitelline blood vessels of some foetuses ligated, antitoxin could be detected in the serum of foetuses whose vessels were not ligated. Those with ligated vessels had no antitoxin in their serum. Thus, in the guineapig, antitoxin appears to be transferred from mother to foetus by way of the vitelline blood vessels. *May F. McCallum*

ENGELBERG, J. **Notes on the Mathematics of the Antigen-Antibody Double Diffusion Technique.** *J. Immunology.* 1959, May, v. 82, No. 5, 467–70.

OSLER, A. G. **Quantitative Studies of Complement Fixation.** *Bact. Reviews.* 1958, Dec., v. 22, No. 4, 246–66, 4 figs. [123 refs.]

This review article is concerned with the development over the past 20 years of improved procedures for determining complement (C′)-fixation and with the knowledge acquired by the use of these improved procedures in the estimation of antigens and antibodies and the investigation of their mode of interaction in highly dilute solution. The author uses the results of his own work in this field during the past 10 years to illustrate the topics discussed.

The emergence of techniques based on a quantitative approach to C′-fixation is described and their limitations are examined. Although these improved methods may not be directly applicable to the work of a clinical laboratory they have been fruitful in the application of the C′-fixation reaction to a number of immunochemical problems. Some of the fields in which quantitative C′-fixation techniques have yielded valuable results are surveyed.

The first topic dealt with is the demonstration of similarities between the processes of C′-fixation and specific antigen-antibody precipitations. Next follows a discussion of the results of investigations into the relationship between the C′-fixing potency and the antibody content of sera. Other topics discussed are the estimation and characterization of antigens by quantitative C′-fixation methods, and the sensitivity of C′-fixation tests. Finally, the author speculates on the future of the C′-fixation test and its applications.

R. B. Morrison

DRESSLER, O. Immunchemische Studien über das Properdinsystem. [**Immunochemical Investigations on the Properdin System**] *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1959, June, v. 117, No. 6, 450–81, 5 figs. [25 refs.]

The English summary appended to the paper is as follows:—

"Immunochemical investigations on the properdin system.

"1. A method for the determination of properdin in sera is described, which is based on the method of Pillemer to determine C'3 after the binding of properdin to zymosan. The determination of the complement level is performed by a multiple point analysis and plotting of hemolysin values in a logarithmic system. The standard deviation of properdin assays was less than ± 10 per cent, and of complement titers less than ± 2 per cent.
In healthy persons no relation exists between properdin and complement levels. The properdin level of healthy persons varies between 2 and 20 per cent, but is very constant in the individual.

"2. The determination in mice of properdin levels is so difficult, showing a standard deviation of about 25 per cent, that the mouse is an unsuitable experimental animal for properdin studies.

"3. The RP reagent prepared from human or guinea pig sera proved to be unsuitable for properdin determination in guinea pig sera. A fraction prepared from pig sera by alcohol precipitation containing C'3 but no properdin, was used as RP reagent together with C'142 from pigs and sheep red blood cells sensitized with rabbit hemolysin. The reference system for the determination of properdin levels in pig and guinea pig sera are standard sera of the same species. The levels obtained are only of comparative significance within the same species. The technical differences do not allow comparison with properdin levels in man.

"4. An assay of properdin in rats could be performed using human RP in a similar way to that in human serum. But the relative high properdin titer thus attained does not lend itself for comparison with the properdin levels in man. This, however, would be possible if an RP from rat serum could be used which to prepare has not yet been possible. It is for this reason that a rat-standard serum was established."

PAULISSEN, L. J. & SHECHMEISTER, I. L. **The Effect of Sublethal Whole-Body X Radiation on Active Immunity.** *J. Infect. Dis.* 1958, Sept.–Oct., v. 103, No. 2, 188–95. [36 refs.]

2 groups of mice, one actively immunized with *Salmonella enteritidis* the other not immunized, were given sub-lethal, whole-body X radiation before being intraperitoneally injected with living suspensions of *Salm. enteritidis*. Although in both groups the resistance to infection was lowered by X radiation, the LD50 for the immunized group was significantly greater than that of the non-immunized group. The protection against infection given by immunization was not destroyed by X radiation. *Elizabeth M. Harper*

NELSON, D. S. & NELSON, R. A., Jr. **On the Mechanism of Immune-Adherence. I. Differentiation from Acid-Adhesion of Bacteria to Erythrocytes.** *Yale J. Biol. & Med.* 1959, Feb., v. 31, No. 4, 185–200, 5 figs.

This paper describes a phenomenon termed "acid-adhesion", which consists of the adherence of particulate antigens (various micro-organisms, starch granules) to erythrocytes. The phenomenon may, under certain conditions, mimic the better-known immune-adherence reaction, in which antigens sensitized with antibody and complement adhere to erythrocytes, and the present account describes various features of the 2 reactions, showing how they may be distinguished. The 2 chief differences are the effect of *p*H, and the role of antibody and complement. Acid-adhesion occurs only at *p*H below 5, whereas immune-adherence is constant over a wide range (*p*H 4–9). Acid-adhesion is dependent upon a change induced in erythrocytes by incubation in an acid medium: this change is reversed by raising the *p*H to 7·5, but once acid-adhesion has occurred (in an acid medium) it is not reversed by raising the *p*H. Immune-adherence occurs only when an antigen is sensitized with antibody and complement: such sensitization is not necessary for acid-adhesion, although it alters slightly the conditions under which acid-adhesion occurs. Immune adherence occurs only with a narrow range of indicator particles—primate erythrocytes and certain non-primate platelets, whereas acid-adhesion occurs with the erythrocytes of many species (chicken erythrocytes are preferred as they are less grossly distorted by acid), with human and rabbit platelets, monkey kidney cells and *Escherichia coli*. Pre-treatment of erythrocytes with tannic acid or trypsin inhibits their participation in immune-adherence, but not in acid-adhesion. The rate of acid-adhesion is rapid and independent of temperature between 0–37°C.: the rate of immune-adherence increases with temperature within this range. High concentration of salts inhibit acid-adhesion but not immune-adherence.

It is concluded from these observations that acid-adhesion is primarily due to an electrostatic bond whereas immune-adherence is due to some other (unspecified) type of bond. *J. R. Anderson*

NELSON, R. A., Jr. & NELSON, D. S. **II. Analogy to Mixed Aggregation of Sensitized Antigens in the Presence of Complement; Immune-Adherence with Animal Platelets.** *Yale J. Biol. & Med.* 1959, Feb., v. 31, No. 4, 201–12, 1 fig. on pl. [41 refs.]

As in the previous paper, the authors are concerned with distinguishing immune-adherence from phenomena which may be confused with it. A reaction termed "complement-dependent mixed aggregation" is described in which 2 particulate antigens, each sensitized with antibody, form mixed aggregates in the presence of complement. In the immune-adherence phenomenon, in which an antigen sensitized with antibody and complement adheres to a non-sensitized indicator particle (primate erythrocytes or certain non-primate platelets), it is important either to ensure that neither the antibody

serum nor the complement serum contains antibody which reacts with the indicator particles, or to wash the sensitized antigen before mixing with the indicator particles. If these precautions are neglected, there is a danger that adhesion may occur between sensitized antigen and accidentally sensitized indicator particles as a result of complement-dependent mixed aggregation. The authors consider that this may explain reports in which immune-adherence has been described with indicators other than primate erythrocytes and non-primate platelets.

To explain complement-dependent mixed aggregation it is postulated that either complement or one of its components is polyvalent, linking together 2 sensitized antigen particles, or that the 2 antigens sensitized with antibody and complement are linked by conglutinin.

In a second part of the paper, confirmation is provided that guineapig platelets can participate, as the indicator particles, in immune-adherence, whereas human platelets are inactive in this respect. *J. R. Anderson*

PONTECORVO, M. Manifestazione della attività del sistema properdinico a mezzo della reazione di immuno-aderenza. **[Manifestations of Activity of the Properdin System in the Course of the Immune-Adherence Reaction]** *Riv. Istituto Sieroterap. Ital.* 1959, Mar.–Apr., v. 34, No. 2, 156–60.

The English summary appended to the paper is as follows:—

"During the course of an investigation on immune-adherence (I-A) of crude diphtheria toxoid-antitoxin with human erythrocytes some observations have been made that indicate the presence of normally occurring reacting substance(s) in the guinea-pig serum being used as C′ source.

"Further experiments have shown that I-A occur with normal guinea-pig, rabbit, mouse, rat, monkey and human sera against different soluble antigens including bacterial polysaccharides.

"The activity appears to be the resultant of a heat-labile component present in the sera; the sera treated with zymosan at 17°C (RP) are hemolytically active and devoid of I-A activity; addition of P to RP restores this activity.

"These results suggest that the non specific heat labile I-A factor may be identified with Pillemer properdin.

"Since evidence to date indicates that both antibody and complement are required for I-A these results may be considered as ancillary data to the investigations of Nelson and others which support the concept that many of the characteristics of properdin could be explained on the basis of low levels of antibody in normal serum."

PIÉRON, R. & BARRETO, M. D. Nouvelles recherches sur la réaction d'immune-adhérence. **[New Work on the Reaction of Immune Adherence]** *Rev. d'Immunologie.* 1959, Jan.–Mar., v. 23, Nos. 1/2, 61–73. [29 refs.]

The following is a translation of the authors' summary:—

"This test with *Escherichia coli* is constantly positive even in healthy persons, and is of no value for the diagnosis of *E. coli* infections.

"On the other hand, when *Bacillus megaterium* is used, the test is only inconstantly and feebly positive, which indicates that certain non-pathogenic bacteria have only a feeble property of adherence.

"Study of this reaction applied to *E. coli*, to staphylococci and to *B. megaterium*, after they have been exposed to heat or proteolytic enzymes, together or separately, suggests that the antigen responsible for the reaction is not protein, or at least that it forms part of the structure of the bacterial wall which cannot be separated by these means." *Charles Wilcocks*

WARDLAW, A. C. & HOWARD, J. G. **A Comparative Survey of the Phagocytosis of Different Species of Bacteria by Kupffer Cells. Perfusion Studies with the Isolated Rat Liver.** *Brit. J. Exper. Path.* 1959, Apr., v. 40, No. 2, 113–17.

The influence of heated and unheated serum on the phagocytosis of 6 Gram-negative and 7 Gram-positive strains by Kupffer cells was studied by using a liver perfusion technique [this *Bulletin*, 1959, v. 34, 839].

The 3 flagellated Gram-negative strains (*Escherichia coli*, *Pseudomonas pyocyanea*, and *Proteus mirabilis*) were phagocytosed in Ringer-Locke solution but the 3 non-flagellated strains (*Klebsiella pneumoniae*, *Salmonella gallinarum*, and *Bacterium alkalescens*) were not phagocytosed from this medium. All 6 were taken up to approximately the same extent from normal serum and heating the serum reduced its opsonic activity in each case.

4 of the Gram-positive strains (*Staphylococcus aureus*, *Bacillus cereus*, *Corynebacterium murium*, and *Streptococcus pyogenes*) showed a very high uptake (nearly 85%) from Ringer-Locke solution. When suspended in heated or unheated serum this uptake was reduced. The 2 clostrida tested behaved like some members of the Gram-negative group, and a capsulated pneumococcus was not phagocytosed from any of the 3 media tested. *Sheila McDonald*

HALPERN, B. N. **The Role and Function of the Reticulo-Endothelial System in Immunological Processes.** *J. Pharmacy & Pharmacol.* London. 1959, June, v. 11, No. 6, 321–38, 15 figs. [38 refs.]

FURNESS, G. & FERREIRA, I. **The Role of Macrophages in Natural Immunity to Salmonellae.** *J. Infect. Dis.* 1959, Mar.–Apr., v. 104, No. 2, 203–6, 3 figs.

In a recent paper the senior author [Furness, this *Bulletin*, 1959, v. 34, 565] showed that when cell cultures of mouse macrophages and a phagocytic strain of altered monkey kidney cells were infected with virulent strains and avirulent strains of *Salmonella typhi-murium* the avirulent strains, after phagocytosis, did not multiply. On the other hand, although some of the virulent bacterial cells were killed those that survived multiplied.

The present paper describes an extension of this work to include macrophages from the rat and guineapig in addition to those of the mouse, for which animals *Salm.*

typhi-murium is regarded as pathogenic. Strains of *Salm. paratyphi B* to which all these animals are naturally immune was also included in the experiments. The results obtained with material from rats and guineapigs were of the same order as those with mouse macrophages. The avirulent *Sa'm. typhi-murium* and the *Salm. paratyphi B*, after ingestion, by mouse, rat and guineapig macrophages were killed within 3 hours. But whereas many bacterial cells of the two virulent strains used were killed after ingestion by the mouse and rat cells only one of these strains appeared to be affected by the guineapig cells. In other words the macrophages of the guineapig had the power of differentiating between two virulent strains of *Sa'm. typhi-murium*. It is suggested that where a strain of salmonella is non-pathogenic for one animal species, but pathogenic for another, the natural immunity of the former species can be attributed to the ability of its phagocytic mononuclear cells to inhibit the multiplication of ingested and potentially virulent organisms. *H. J. Bensted*

KRYLOV, V. N. **An Analysis of the Physiological Basis of So-called Depression Immunity. II. Manifestations of Depression Immunity during Temporary Functional Inhibition of the Central Nervous System.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, No. 10, 1552–7. [Translated from Russian.]

MATEWA, Vera. Titrierung von Phenol-Tollwutimpfstoffen nach den Methoden von Habel und Krause. [**A Comparative Study on the Titration of Phenol Type Rabies Vaccines, according to the Methods of Habel and Krause**] *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 175, Nos. 1/2, 55–8, 1 fig.

——. Titrierung des mit dem Stamm Flury hergestellten Tollwutimpfstoffen. [**Titration of Rabies Vaccines prepared with the Flury Strain**] *Ibid.* 59–62.

[Abstracts of these papers appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 939.]

ORLOVA, N. N. **A Study of Dried Formolized Rabies Vaccine adsorbed on Calcium Phosphate.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, Nos. 1/2, 194–9, 1 fig. [Translated from Russian.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 940.]

Miscellaneous

CHALKE, H. D. & WATTON, R. W. **Home Accidents: a Survey in a Metropolitan Borough.** *Med. Officer.* 1959, Apr. 24, v. 101, No. 17, 225–7.

The chief aim of this home accident survey in Camberwell "was to discover the incidence, nature and causes of the less serious accidents particularly those occurring in the middle years of life. These appear to be of particular importance from a preventive standpoint". Information was obtained from the 2 general hospitals which serve the borough, general practitioners and by means of visits by public health inspectors and health visitors. In the period covered—July 1957 to October 1958—the returns from the hospitals were for 750 persons of whom 94% received out-patient attention only. These accidents were analysed and the numerical data are set out in tables by age-group, sex, type of accident and per 100 of population at risk.

"The figures from this survey in Camberwell are in general agreement with previous studies." [This *Bulletin*, 1954, v. 29, 217.] The greater prevalence of accidents in the female than in the male after the age of 15 years was very marked as, for example in the 21–45 age-group there were 35 accidents in men and 130 in women. The types of accident in order of numerical importance were falls (372), cuts (170), burns and scalds (139), swallowing tablets, poisonous liquids or foreign bodies (35), electric shocks and burns (4), coal-gas poisoning (1) and miscellaneous (29).

There is a good discussion in which there is reference to the value of reporting accidents by hospitals and general practitioners and also observations on methods of prevention of accidents in the home.

M. E. Delafield

COOKSON, J. S. & MACLAY, D. T. **Home Accidents in Under-Fives. A Survey in Herefordshire.** *Med. Officer.* 1959, Apr. 24, v. 101, No. 17, 227–9.

This investigation of home accidents in children under 5 years of age was based on reports in 1958 from the Hereford General Hospital and the Hereford County Hospital. These hospitals are the only ones in the county which undertake the treatment of a substantial number of home accidents. In 1958 there were 85 accidents in children under 5 which is an annual rate of 8·8 per 1,000. Of these 31 were girls and 54 boys. These figures are analysed shortly by age, severity of accident and social class of the family. All the families were visited by health visitors from whom information was requested about the psychological make-up of both child and mother under such headings as whether the child is intelligent or happy or not and the mother affectionate or easy in manner or impulsive or the opposite. From an analysis of the figures obtained it is considered that "The psychological make-up of the child does not appear to be of any special significance, but quite clearly there is a type of mother who is

anxious, over-meticulous and hypochondriacal, whose child is more likely to have an accident."

M. E. Delafield

MORFITT, J. M. **Home Accidents in Young Children. A Survey in Doncaster.** *Med. Officer.* 1959, Apr. 24, v. 101, No. 17, 229–33, 2 figs. [12 refs.]

This is a detailed account of a survey of home accidents in children under 5 years based on reports from the Doncaster Royal Infirmary where all accidental injuries occurring in the County Borough are treated. The investigation covered the period February, March, April and May, 1957 and during this period 103 children under 5 years of age suffered 106 injuries requiring hospital treatment. This figure represents an incidence of 13·9 per 1,000 in 4 months. All the homes where accidents had occurred were visited by the author and then by a health visitor. From the information so obtained there is a description (with tables) of the findings which are compared with the results recorded in other published work. Accidents were most frequent at ages 2–3 and 3–4 years. 60 accidents were in boys and 43 in girls. Study of the hourly distribution showed peaks of incidence at 12 noon to 12.59 p.m. and at 6 p.m. to 6.59 p.m. Accidents occurring indoors were about equal in number to those happening outdoors. Most of the " accident mechanisms " were falls (68 cases) and there were only 4 scalds and 1 burn. Sex incidence by type of injury and the situation of the lesions are also described.

The causative factors—faulty design and equipment in the home and " human frailty " of child or parents—are well described and discussed in particular relation to accident prevention. *M. E. Delafield*

MEDICAL OFFICER. 1959, Apr. 24, v. 101, No. 17, 233–6. **" Operation Jane " at Worthing. An Experiment in Home Safety Education, 1st May to 31st July, 1958.**

In 1958 the Worthing Home Safety Committee decided to carry out a project similar to an educational experiment made in the small town of Corrigin which had been conducted by the Western Australian Health Education Council in order to bring down the incidence of accidents in the home. The Worthing project called " Operation Jane " was designed to obtain information on Home accidents and " at the same time to provide a method of changing or improving family attitudes towards safety in the home ". Record sheets asking for simple answers to 12 questions and records for 3 months were prepared and enclosed each in a wallet with selected leaflets on safety in the home. These were delivered to 1,036 homes by the agency of 100 voluntary stewards and collected by them after 3 months. A total of 672 of the forms were completed and returned. The Committee express their appreciation of the excellent assistance given by the Press and the help of many individuals and organizations. The data obtained which cover a total of 2,191 persons in the survey are set out in a series of tables. A total of 515 (23·5%) persons reported accidents and of these 452 were of minor grade, 42 were mild and 21 severe. Projecting this experience to the whole population of Worthing could mean a yearly total of 17,000 accident injuries of which 400 would require hospital treatment. Other tables set out the accident data obtained in the survey by weekly rate, sex, age, location in the home, time of day, by type of injury (most prevalent were 384 cuts and bruises and 89 burns and scalds), by part of body affected, by cause (falls were the most frequent) and incidence per household. *M. E. Delafield*

HUME, C. W. **The Strategy and Tactics of Experimentation.** *Lancet.* 1957, Nov. 23, 1049–52. [23 refs.]

The author, as Secretary General of the Universities Federation for Animal Welfare, contributes an engaging plea for better experimentation which would provide as much information by the use of fewer laboratory animals. In *strategy* he calls for a higher ratio of thinking to experimenting, for less trial and error and for more insighted following of clues. This part of his essay could be read with benefit by many research workers. In *tactics* he calls for better experimental design and the use of more sensitive methods of analysis. Here his rapid review of the field is likely to be confusing to the uninitiated and unnecessary for the converted, particularly as he has made a mistake in the calculation of the exact probability by Fisher's method, and contrary to his statement, has chosen for his example a table in which the conventional χ^2 test is entirely adequate. *J. Knowelden*

HABERMANN, R. T. **Spontaneous Diseases and their Control in Laboratory Animals.** *Pub. Health Rep.* Wash. 1959, Feb., v. 74, No. 2, 165–9.

This paper summarizes a large-scale investigation done during the past 10 years at the United States National Institutes of Health on the natural diseases of mice, rats, guineapigs, rabbits and hamsters in captivity.

The surface and internal parasites of each of these animals are discussed, and details are given of methods of treatment. The incidence of salmonellosis and its prevention by strict sanitary measures are considered in general terms. Experiments on the control of chronic respiratory disease of rats are presented in considerable detail. They showed that regular administration of sulphamerazine in the feed eliminated the disease by the third generation of rats so treated. Epidemic diarrhoeal disease of suckling mice, snuffles and mucoid enteritis of rabbits, and lymphadenitis and salivary gland disease of guineapigs are considered briefly.

[This paper is a useful review of the subject; though fairly short it contains much detailed information which cannot be given in an abstract.] *I. B. R. Duncan*

Book Reviews

BENJAMIN, B. [B.Sc., Ph.D., F.I.A., F.S.S.]. **Elements of Vital Statistics.** 352 pp., illustrated. 1959. London: George Allen & Unwin Ltd., Ruskin House, Museum Street, W.C.1. [56s.]

This book resulted from an attempt to revise and bring up to date NEWSHOLME'S classic *Elements of Vital Statistics*, which is out of print, to replace it for the same circle of readers. The book requires no knowledge of statistics or mathematics and no attempt has been made to introduce methodology. Algebraic symbols only appear in a few places, mainly in the chapter on "Mortality Indices: Life Tables". The descriptive style adopted by Newsholme has been followed but the presentation is somewhat different, reflecting, perhaps, the difference in points of view of an actuary and a medical officer who was a teacher.

The first 7 of the 18 chapters deal with population, registration of deaths, births and marriages and with mortality rates and causes, and the remaining chapters with morbidity generally, including maternal and child welfare, health of the school child and industrial and general incapacity. The recent developments in the field of vital statistics including the systems of registration of cancer and mental disorders and hospital statistics are dealt with in detail. The chapter on tuberculosis reviews the tuberculosis services, the problems of control, follow-up, the defects in notifications, and the difficulties in making local comparisons of notifications.

A brief but concise history of the census, the registration of births, marriages and deaths, and the notification of infective diseases precedes the chapters dealing with these topics.

The methods of registration, collection and presentation of statistics in America are contrasted with England and Wales for some indices. The validity of international comparisons and the recommendations of international bodies on classification are considered.

An extensive list of references after each chapter for readers who wish to extend their studies forestalls the reviewer's criticism that some aspects might have been dealt with at greater length. [Despite this he thinks that Chapter 8 on the Measurement of Morbidity is sketchy and might profitably have been expanded, especially as in the future morbidity will play a larger part in the planning of health services and hospital needs.]

The author has achieved a very large measure of success in his attempt to bring together within a small compass all the relevant facts on vital statistics. The book contains a mass of information, gathered from many sources, that is important to all interested in vital statistics and their use and will form a useful book of reference.

W. J. Martin

MAY, Jacques M. [M.D.]. **The Ecology of Human Disease.** With a foreword by Felix MARTI-IBANEZ, M.D. pp. xxiv + 327, illustrated. 1959. New York 22: MD Publications, Inc., 30 East 60th Street, N. Y. [$7.50.]

In a largely philosophical foreword contributed by Professor Marti-Ibanez, a distinction is made between the history and geography of disease, historical and geographical pathology, historical and geographical medicine and the ecology of human disease. This last indicates a wide philosophical perspective of medical thought in which disease is conceived as a convergence in time and space within the person of the patient of organic, inorganic, or social-cultural stimuli. The challenge of these stimuli induces a tissue response which represents disease, whether communicable, degenerative or behavioural, and which in its turn eventually results in ecological adaptation and the survival of the species or continuing maladjustment leading to elimination of the species. In the main text, Dr. May defines disease as that alteration of living tissues that jeopardizes their survival in their environment. It is thus a temporary state of the living cell in conflict with environmental challenges, trying to cope with them and survive, and it follows that characteristics of the cell which might be favourable in some environments could be adverse in others. He then examines the challenges, direct and indirect, organic and inorganic, which constitute the stimuli. The response to them by the tissues is in part due to the genotypic and in part to the phenotypic characteristics of the individual. There are then briefer statements on the nature of the barriers which impede the movement of disease in the individual or between individuals, on the nature of races of mankind, on cultural factors, and on the general changing characters of disease. This philosophical introductory account is succeeded by a series of chapters dealing with the ecology of cholera, brucellosis, poliomyelitis, leprosy, bacillary dysentery, the salmonelloses, amoebiasis, yaws, 3 worm infections, scarlet fever, measles and (contributed by Mathieu-Jean FREYCHE) trachoma.

These studies follow a pattern of brief introduction, definition of disease, description of the aetiological agent, the reactions of the host and an account of the geographical distribution of the disease which is in some cases very detailed and lengthy. A discussion follows on the geographical distribution with some examination of the factors which have caused it. Each of these chapters is in its own way good. They appear to the reviewer to constitute straight accounts of historical and geographical pathology, bringing together much which would be difficult to collect from other sources in an interesting and authoritative and well-written manner. They are, however, slightly disappointing as elaborations of the philosophical conception outlined in the earlier parts of the book. One had been led from both the foreword and the introductory chapters to expect an entirely novel approach. To think, for instance, of poliomyelitis in terms of the influence of external factors on the transmission of the virus, and then of the relation between previous stimulation of the motor-neuron and its survival under challenge from the virus, proceeding from these two approaches to an analysis of the nature of geographical distribution and the distribution of paralysis in different parts of the body. Geographical distribution of the disease, however, receives a vague examination

which leads to the conclusion that we cannot explain the pattern shown on the maps: the examination of the distribution of paralytic lesions is limited to the statement that the causes governing the localization of the virus in this or that group of neurons are not understood, though it could be due to certain strains of virus specifically requiring various chemical environments found in different neurons. The introductory sections also led to ideas on the analysis of the immediate surroundings in which tuberculosis occurs and the susceptibilities of different individuals, but discussion of these matters proves to be very limited. The account of host susceptibility deals almost exclusively with heredity, pregnancy and BCG vaccination, and the discussion on geographical distribution is very brief. Perhaps the very high ambitions of the start are not quite achieved, but this does not detract seriously from the value of a book which contains much collected material of considerable interest and which deserves study by those with either an ecological outlook or with an interest in historical and geographical pathology. *G. Macdonald*

PAUL, John R. [M.D., Sc.D.]. **Clinical Epidemiology.** pp. xii + 291, 37 figs. 1959. Chicago 37: University Press, Bently House, 200, Euston Road, N.W.1. [37s. 6d.]

Dr. Paul is Professor of Preventive Medicine at Yale University. This introduction to epidemiology for doctors and students incorporates much of the substance of his own lectures and practical experience. The first part is an historical introduction, the second part deals with principles and methods, and the third and last part deals with "sample" diseases. The author contends that for the newcomer to epidemiology "it is easier to begin with infectious disease", and admits that he has neglected to deal so fully with other medical fields. Unfortunately, this selective approach quite misleads the reader about the scope of the subject. A whole chapter, for instance, is devoted to arthropod-borne virus diseases, while the only mention of the possible effects on health of atmospheric pollution is a historical reference to SYDENHAM's concern with the atmosphere of London.

No doubt the object has been to encourage the young clinician or student to look beyond the bedside, and not to frighten him with statistics. Observations are cited, such as those of ZENKER and PICKLES, who were able to trace the route of transmission of infectious disease by simple observations and charting of the results. But such unifactorial situations are, regrettably, a less and less important source of new fundamental knowledge. More and more of the interesting and baffling problems in public health are now those of the degenerative diseases of middle life, whose aetiology is complex and cannot be so simply determined. The author himself emphasizes that epidemiology is concerned no longer only with the control of epidemics, but also with the ecology of disease and the interaction with host factors of the total environment. Yet he has not mentioned the most urgent need of the clinical epidemiologist in this new setting. This is a critical attitude to numerical data, without which attempts at investigation will soon lead to frustration and unproductive work. By this attempt at "epidemiology without tears" Dr. Paul has underrated the interest and the ability of young medical men in simple statistical methodology.

This book is both readable and short, and these are commendable assets. It is written in a lively and conversational style. The descriptions of particular studies, the illustrations, the chapter describing graphic methods of presenting data and the historical introduction are excellent. Those interested in the epidemiology of infectious disease will find it valuable and stimulating, but others may want to look elsewhere for a better proportioned and more comprehensive account of the subject. *A. S. Fairbairn*

KÖHLER, W. **Die Serologie des Rheumatismus und der Streptokkeninfektionen.** [The Serology of Rheumatism and Streptococcal Infections] 2nd Edition. *Beiträge z. Hyg. u. Epidemiol.* Leipzig. 1959, No. 9, pp. x + 227, 16 figs. [957 refs.]

The 1st edition of the monograph, with the title *Streptolysin and Antistreptolysin Reaction,* was reviewed in this *Bulletin* [1957, v. 32, 622]. In the 2nd edition the scope has been widened to deal with antibody reactions to fibrinolysin and hyaluronidase and with the so-called L- and O- streptococcus agglutinations reactions, the haemagglutination reactions (*e.g.* Rose-Waaler) and the C-reactive protein. The scheme of the book remains the same. In each case the nature of the antigen is discussed and the method of testing for its antibody described, together with definitions of the units in which the results are reported. There are extensive tables summarizing reported values of the antibody titres found in normal individuals in various countries and at various ages, as well as those found in various diseases. The results for antistreptolysin naturally occupy the greatest space. Techniques for the various tests are described in detail.

The criticisms offered of the 1st edition are valid for the 2nd: there is far too little discussion of the possible fallacies in comparing results collected from many disparate sources; and the section on interpretation—of all the reactions—occupies only 2 pages. The usefulness of the tables for quick reference is diminished by the fact that many of them have no headings, so that their implication has to be sought in the text. Nevertheless, the value of the book, as a comprehensive review is very great, and the number of references quoted is now 957. *R. E. O. Williams*

LAURENCE, D. R. [M.D.] [Edited by.] **Quantitative Methods in Human Pharmacology and Therapeutics. Proceedings of a Symposium held in London on 24th and 25th March, 1958.** pp. xvii + 253, illustrated. 1959. New York. Paris. Los Angeles. London: Pergamon Press Ltd., 4 & 5, Fitzroy Square, W.1. [45s.]

The therapeutic value of discoveries made by experiments on animals can only be settled by tests on human beings, and this book is the record of a symposium designed to bring together clinical and laboratory workers who had a common interest in the measurement of drug effects in man. Quantitative procedures which

can be employed in human pharmacology have been notably improved in recent years, a consideration which made the choice of subject very timely. Participants in the symposium included well-known pharmacologists and experimental statisticians from Europe and North America, who contributed 21 papers on the evaluation of drugs in man; 11 of these deal with methods and problems, 6 with newer statistical techniques, and 4 with the introduction of drugs into clinical practice and clinical trials. The papers include useful reviews of methods of assessing changes associated with particular types of drug action, covering subjects such as the measurement of physiological variables (A. C. DORNHORST, pp. 11–15); the effects of thyroid hormones (R. PITT-RIVERS and W. R. TROTTER, pp. 16–23); neuromuscular block (E. ZAIMIS, pp. 24–30); the effects of drugs on the gastro-intestinal tract (E. N. ROWLANDS, pp. 31–39); analgesia (C. A. KEELE, pp. 57–68); muscular concomitants of emotion (P. SAINSBURY, pp. 69–75); and the effects of drugs on performance and incentives (H. STEINBERG, pp. 76–87) and on motor activity (L. GOLDBERG, pp. 88–97). Other valuable contributions were a paper by H. GOLD (pp. 40–54) on experiences in human pharmacology and one by H. K. BEECHER (pp. 98–116) on the measurement of subjective states. The section on newer statistical methods should be of great interest to all pharmacologists; as J. H. GADDUM (pp. 3–10) remarked in an admirable introduction, "If you are not a professional statistician there is no need to understand statistics, but it is important to know what statistics can do for you." The final section contains thoughtful and constructive discussions of factors which have to be taken into account when planning clinical trials in man, the important ethical aspects receiving special attention.

This collection of papers and the records of discussions which followed them should provide stimulating reading for clinicians and laboratory workers who are concerned with the development of reliable techniques for assessing the effects of drugs on man.

R. S. F. Hennessey

POLLARD, Morris [Edited by.] **Perspectives in Virology.** A symposium. pp. xix + 312, illustrated. 1959. New York: John Wiley & Sons, Inc. London: Chapman & Hall Ltd., 37, Essex Street, W.C.2. [56s.]

This symposium was held in New York in February 1958 in memory of the late Dr. F. R. BEAUDETTE.

The contributions cover a very wide field and include papers on Plant Viruses, Animal Viruses, Tumour Viruses and Bacteriophage; each chapter includes a report of the discussion which followed the paper or papers which were read, and these discussions have been exceptionally well edited.

Lawrence KILHAM has provided an imaginative contribution called *Virus Transformation and Cancer* (pp. 54–74). Here it is suggested that cell and cancer virus represent a dual organism which usually remains quiescent, owing to inhibitory influences; procedures used in the isolation of cancer virus may be supposed to remove the inhibitors. There is an interesting account of a virus-induced leukaemia of adult mice by Charlotte FRIEND (pp. 231–244) and a paper on the Polyoma virus by Sarah E. STEWART & Bernice E. EDDY (pp. 245–255); this virus seems to induce a surprising range of tumours in mice.

The discussion which follows these studies of tumour viruses is particularly stimulating.

In an earlier part of the book Werner SCHÄFER (pp. 20–42) gives a plausible, if somewhat speculative, account of the multiplication of some myxoviruses. [It is unfortunate that the same author gave a very similar contribution illustrated by the same diagrams and photographs to the more recent symposium on *Virus Growth and Variation* held in London in April 1959.]

There is a useful chapter by Theodore T. PUCK on *Quantitative Measurement of Virus Action by Cell Plating Techniques* (pp. 88–102) and a good review by John F. ENDERS and his colleagues of *Recent Advances in Knowledge of the Measles Virus* (pp. 103–20).

René DUBOS contributes a delightful epilogue entitled *Tulipomania and the Benevolent Virus* (pp. 291–9).

The book is well printed and illustrated, and it can be recommended particularly because of its wide scope.

Forrest Fulton

WORLD HEALTH ORGANIZATION. **World Directory of Venereal-Disease Treatment Centres at Ports. Application of the International Agreement of Brussels, 1924, respecting Facilities to be given to Merchant Seamen for the Treatment of Venereal Diseases.** 162 pp. 1959. Geneva: Palais des Nations. [Sales agent for U.K., H.M. Stationery Office.] [8s. 6d.; $1.75; Sw.fr. 5.–.]

INTERNATIONAL LABOUR OFFICE. **African Labour Survey.** pp. xiv + 712, 1 map. Studies and Reports New Series, No. 48. 1958. Geneva. London: 38–39, Parliament Street, S.W.1. [$5.00: 30s.]

Most of the territories in Africa south of the Sahara are passing through an industrial revolution involving substitution of an internal exchange economy for a subsistence economy, wage-earning for peasant farming, and congregation in towns and labour lines for life in dispersed rural communities. A survey of labour conditions there, undertaken at the instigation of the International Labour Office, is reported here. Since the problems encountered and the services introduced differ according to territory the report has 3 objects: to depict present conditions in Africa as a base line for future surveys; to provide information concerning the way in which common problems are being dealt with by various territories; and to contribute to the general understanding of the social and economic problems of that continent.

The report is presented in 16 chapters accompanied by 5 appendices and an index of references. Certain of the chapters only are of direct medical interest, particularly Chapters 9 to 12 dealing with conditions of work, occupational safety and health, social security and workers' housing. In addition, the whole problem presented by the industrial revolution is discussed in general terms in the first chapter where it is stressed that the economic transformation of Africa necessitates a fundamental alteration in the pattern of living and habits of thought appropriate to the traditional environment. The

alteration has to be effected in many cases without passage through intermediate technological stages which facilitated adjustment in other communities now highly developed. This chapter also discusses health and nutrition problems in broad terms and touches on nutritional standards, blindness, tuberculosis, the causes of migration to towns and the social and housing problems which ensue. Interesting discussions on a variety of subjects appear in various other chapters: Chapter 2 comments on factors affecting productivity and thus economic development, and urges better education of women so that they will appreciate and demand higher living standards; medical factors, among others, which affect the productivity of labour are mentioned in Chapter 5; the measurement of poverty is dealt with in Chapter 8, and Chapter 9 compares the practices of different countries in the provision by industry of housing, food and medical assistance to its labour forces; a plea is made in Chapter 10 for planning ahead so that social evolution may occur without the unfortunate sequelae of the industrial revolution in Europe, and it is urged that occupational and health services must be developed locally to meet the problems there, since their transplantation from elsewhere may prove unsatisfactory.

Turning to the chapters which will prove of greatest interest to medical readers, Chapter 11 discusses social security, and points out that the new group of permanently employed persons requires government protection because it no longer has its security ensured by the traditional organizations of family clan or tribe. Even where social security measures have been developed in Africa old age is usually not covered, nor is African unemployment. Tribute is paid to the achievements of the health services which first controlled epidemic disease, then certain endemic diseases and are now interested in the reduction of some important social diseases.

A chapter on housing describes this as one of the key elements in the level of living and one of the most acute economic and social problems of Africa today. The essential requirements of housing policy are described. It is a new concept of human welfare that governments should be responsible for ensuring a decent minimum standard of living involving minimum building standards, and town-planning and building regulations. The great majority of Africans cannot afford an economic rent for a decent house, and the problem is made more difficult by lack of suitable local materials and by complicated land tenure systems. The final chapter summarizes preceding ones. It describes the social objectives of economic development and stresses that the raising of levels of living depends on increased productivity. This would be facilitated by stabilizing the labour force which could be achieved by providing housing, wages sufficient to support a family, welfare services in sickness, accident and old age, and by house ownership. It discusses the difficult problem of deciding the allocation of resources between improving present living standards and promoting fundamental long-term development.

This book will prove particularly valuable to industrial medical officers in the tropics because it explains the underlying reasons for the existence of problems and of difficult attitudes on the part of the African. It describes the experience of others facing the same difficulties and the solutions they have worked out. The medical sections of the book will be of use to everyone concerned with health in Africa and indeed in other parts of the tropics. Those interested in the progress of African peoples towards a higher level of living will find it of value because it deals with the path that must be followed. That is the justification for the doctor reading more than those sections dealing with welfare and health services for workers. The whole series of social and economic problems in the rapidly developing African territories forms a complex which constitutes the background of health problems there. This report illustrates the linkage of poverty and ill-health by pointing out that migrant labour is untrained and hence inefficient, and in consequence wages are low and housing and food poor. The report contains a vast amount of detailed information about the social organizations and legislation which have stemmed from development in Africa, and thus it is a most useful book of reference concerning the obligations and opportunities of industrial undertakings in welfare work. It is also a book which can be read almost throughout with great interest by those interested in African development. *T. H. Davey*

SOC. EXPER. BIOL. **The Biological Replication of Macromolecules. Symposia of the Society for Experimental Biology No. 12.** pp. vi + 255, numerous figs. [Numerous refs.] 1958. Cambridge: London: Cambridge University Press, Bentley House, 200, Euston Road, N.W.1. [50s.]

This symposium consists of 17 papers covering all aspects of the replication of macromolecules, the definition of which is stretched to the utmost in one instance to cover the multiplication of an animal virus. The individual contributions deal with the formation of nucleic acids, proteins, polysaccharides and enzymes; this review deals only with those topics which will concern medical readers, although there is much of general interest in the remainder. G. PONTECORVO, in his introductory paper *Self-reproduction and All That* (pp. 1–5), establishes the proceedings on a firm footing of lucidity by defining a self-replicating system as one which is necessary for its own replication, and which can give rise to a mutated system which can reproduce in the mutated form. He then discusses the translation of the gene concept into biochemical terms, and infers that in *Aspergillus* and *Drosophila* the smallest element which can undergo recombination is a series of 8 nucleotide pairs, and that the gene consists of an array of 100–10,000 nucleotides. The fractionation of deoxyribonucleic acid is discussed by G. L. BROWN and A. V. BROWN (pp. 6–30); the material from most sources is a complex mixture, but a single chemical species of deoxyribonucleic acid can be isolated from T2 phage which appears to carry the genetic determinants which control the tail protein which is responsible for the host-range. The theoretical possibility thus exists of comparing the chemical structure of variants of a particular deoxyribonucleic acid and its corresponding variant proteins.

The contribution of F. H. C. CRICK (pp. 138–63) on protein synthesis is worthy of detailed study, since the

basic concepts of the problem are presented with a clarity and simplicity, which while effectively concealing the formidable intellectual difficulty, nevertheless render this field of investigation readily accessible to the inexperienced. It is pointed out that the main function of proteins is to act as enzymes, and an account is given of their amino-acid composition, homogeneity and structure. It is always taken for granted that nucleic acids control the synthesis of proteins, but the evidence for this is so far very meagre and depends upon a few specific instances. The first step in protein synthesis is probably the activation of each amino-acid by an individual activating enzyme which couples it with adenosine monophosphate, after which the activated amino-acid is transferred to the microsomes. In conclusion Crick crystallizes ideas on the mechanisms of protein synthesis into 2 principles, the sequence hypothesis, which states that the specificity of a nucleic acid resides in the sequence of the bases, which corresponds to the sequence of amino-acids in a particular protein, and the central dogma, which postulates that once information has been transferred to a protein it cannot get out again, *i.e.*, the amino-acid sequence of the protein cannot function as a code to control the sequential structure of subsequently formed macromolecules. The original hypothesis that nucleic acids possessed cavities which fitted specific amino-acids and thereby controlled the sequence has been found to be untenable, and it is now considered that small molecule adaptor compounds must intervene between the nucleic acids and the amino-acids which they are thought to control. The original hyopthesis of GAMOW on the coding of the information transfer has now been disproved from a study of known sequences of amino-acids, such as those of the insulin molecule, and Crick puts forward another code by which combinations of 4 nucleotides can be associated with precisely 20 amino-acids and no more.

Interesting advances in knowledge of the biosynthesis of oligo- and polysaccharides are described by M. STACEY (pp. 185–94), although these compounds strike the medical reader as prosaic in comparison with the intellectual appeal of the proteins and nucleic acids. A subject of more immediate medical importance, the induction of enzymes in bacteria, is discussed by M. R. POLLOCK and J. MANDELSTAM (pp. 195–204). The topics reviewed so far are no more than a limited selection of those dealt with in this book, and the medical reader will also find much of interest in a number of other contributions.

D. J. Bauer

ADAMS, Mark H., with E. S. ANDERSON, J. S., GOTS, F. JACOB & E. L. WOLLMAN. **Bacteriophages.** pp. xviii + 592, illustrated. 1959. New York 1: Interscience Publishers, Inc., 250, Fifth Avenue, N.Y. London: Interscience Publishers Ltd., 88–90, Chancery Lane, W.C.2. [$15.00.]

This is the first book devoted solely to bacteriophages to be published since the revival of interest in the subject 20 years ago. Begun by the late Mark Adams, who died before completing the text, it was finished by a group of distinguished workers in the field, under the editorship of A. D. HERSHEY. The book is on the whole clearly and simply written, and well supplied with references. To quote the preface, it is "reasonably complete, reasonably up-to-date, and reasonably elementary".

An account is given of the morphology of bacteriophages, of their size and how this has been measured, of their composition, both chemical and antigenic, and of their host specificity. There are chapters on the effects of physical and chemical agents. The processes of infection, growth and multiplication in all their stages are dealt with, and also the effect of the phage upon the host cell. J. S. GOTS contributes a chapter on chemical interference with phage growth. There is a section on phage genetics, a subject which has made great advances in the last few years. F. JACOB and E. L. WOLLMAN have written a chapter on lysogeny and another on bacteriocins. E. S. ANDERSON deals with phage typing and its use in epidemiological studies. The appendix consists of Mark Adams's manual on *Methods of Study of Bacterial Viruses*, reprinted and revised. This is the paper most often quoted in current phage literature and it will be a great help to many beginners and others to have it at last made accessible.

This book can be warmly recommended to those studying bacteriology and virology, for whom it will probably become the standard reference book.

Janice Taverne

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